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THE HUMORAL PRODUCTION OF CARDIAC INFARCTS

BY

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It has long been known that, although desoxycorticosterone itself does not cause nephrocalcinosis, it does produce favourable conditions for the production of this lesion by the concurrent administration of in themselves inactive doses of phosphates (Selye *et al.*, 1945). This typical instance of "conditioning" by a hormone for the potentially pathogenic actions of an otherwise innocuous substance served as a basis for systematic investigations designed to clarify the relationship between the nephrocalcinotic and the other pharmacological actions of steroids (Selye and Bois, 1956a, 1956b).

In the course of more recent studies designed to extend these observations to certain newly synthesized halogenated corticoids, it was accidentally observed that rats treated concurrently with 2α-methyl-9α-chlorocortisol (Me-Cl-COL) and NaH_2PO_4 invariably succumbed with the clinical manifestations of acute cardiac death, and necropsy regularly revealed large, yellowish, infarct-like necrotic patches in their myocardium (Selye, 1957a). Subsequent investigations showed that, histologically, these lesions also resemble the true spontaneous cardiac infarcts of man: like the latter, they consist of large, sharply delimited foci in which the myocytes first disintegrate and are then invaded by histiocytes and polymorphonuclear cells. This similarity is further emphasized by the fact that sudden exposure to stress can precipitate the development of such cardiac necroses in rats pretreated with subthreshold doses of phosphate plus Me-Cl-COL or related steroids (Selye and Renaud, 1957a, 1957b). On the other hand, the experimental lesion essentially differs from ordinary infarcts in that there is a constant absence of any histologically demonstrable vascular occlusion. To emphasize both their resemblance to and distinctness from true cardiac infarcts, these lesions have been referred to (with regard to their appearance) as an "infarctoid cardiopathy"; but to distinguish them from infarct-like lesions due to other causes they are also designated (with regard to their causation) as the "phosphate-steroid-cardiopathy" (Selye and Mishra, 1958).

This experimental disease has been the subject of many investigations during the last year, in the hope that the newly discovered interaction between phosphates and steroids might help to elucidate certain problems of cardiac physiology as well as the puzzling but not uncommon cardiac infarcts which occur, without evidence of acute coronary occlusion, in man (Opitz, 1935; Gross and Sternberg, 1939; Meessen, 1944; Büchner, 1955). Therefore, before proceeding with the description of our original observations, it will be necessary to give a brief synopsis of the scattered and polyglot literature concerned with the pathogenesis and clinical implications of the phosphate-steroid-cardiopathy. These may be summarized under the following five headings.

1. The Electrolyte Component

Our first task was to establish whether it is really the PO_4 moiety of NaH_2PO_4 that is of importance in conditioning the cardiac muscle for the necrotizing actions of steroids such as Me-Cl-COL. Experiments on rats indicated that both NaH_2PO_4 and Na_2HPO_4 (as well as neutral mixtures of both these salts) are highly active in this respect. It was assumed, therefore, that the lesions are not due merely to a change in *p*H induced either by the acid or by the basic phosphate. Since, on the other hand, equimolecular amounts of NaCl, given conjointly with Me-Cl-COL, failed to produce such myocardial necroses, the sodium ion in itself likewise cannot be the responsible conditioning factor. From this it was concluded that, for the production of the phosphate-steroid-cardiopathy, the phosphate ion is the essential part of NaH_2PO_4 (Selye and Renaud, 1958a).

Subsequently, it has also been possible to produce similar cardiac lesions by combined treatment with Me-Cl-COL and other inorganic phosphorus compounds such as NaH_2PO_3, Na_2HPO_3, NaH_2PO_2, $Na_4P_2O_6$, $Na_4P_2O_7$, and $(NaPO_3)_6$. It is of interest that only the last two of these salts share with NaH_2PO_4 and Na_2HPO_4 the property of producing nephrocalcinosis concurrently with the cardiopathy. Hence the development of the cardiac necroses is not merely the consequence of renal calcification (Selye, 1957b). Up to now, only derivatives of phosphoric acid were found to be effective in producing this cardiopathy; yet the specificity of this salt action has still not been fully proved, because meanwhile few other anions have been tested for their ability to produce cardiac necroses when given in combination with steroids.

It is well known that similar cardiac lesions can also occur in rats maintained on potassium-deficient diets (Thomas *et al.*, 1940; Liebow *et al.*, 1941; Follis, 1942). It has been shown, furthermore, that both the phosphate-steroid-cardiopathy and the accompanying nephrocalcinosis can be prevented by oral administration of KCl (Selye and Renaud, 1957a). In view of this, it would have been tempting to postulate that the combined treatment with phosphate and steroid acts through the production of a potassium deficiency. It soon

became evident, however, that the protective effect of KCl is shared not only by $KHSO_4$, K_2SO_4, and CH_3COOK, but also by $MgCl_2$ and, though to a much lesser extent, even by $CaCl_2$, NH_4Cl, and NaCl. These findings suggested that the prophylactic action of KCl is non-specific and perhaps largely due to the accompanying increase in water turnover. However, forced oral administration of water (even when it is given in amounts far greater than those normally taken by the electrolyte-treated animals) exerts little, if any, protective effect against the phosphate-steroid-cardiopathy, while treatment with comparable quantities of an aqueous glucose solution actually aggravates it (Selye and Mishra, 1958). These observations clearly showed that the protective effect of KCl is not entirely specific, but further work will be necessary to determine the characteristics that electrolyte solutions must possess in order to prevent the phosphate-steroid-cardiopathy.

Our next concern was to establish the site of interaction between NaH_2PO_4 and those electrolytes that prevent it from causing the cardiopathy and nephrocalcinosis. Of course, the large amounts of NaH_2PO_4 that are required for the production of these changes cannot be administered subcutaneously, intravenously, or intraperitoneally. It was noted, however, that if, in rats, a large subcutaneous air bubble is prepared, and increasing concentrations of irritants are injected into its lumen, the wall of the resulting "granuloma pouch" becomes unusually resistant to the necrotizing effects of highly hypertonic solutions. Hence we injected the requisite amount of phosphate into subcutaneous granuloma pouches of Me-Cl-COL-treated rats which simultaneously received either $MgCl_2$ or KCl by mouth. Under these conditions, both $MgCl_2$ and KCl still exerted their customary prophylactic effect (Selye, 1957c). These experiments furnished definite proof that the protective salts do not act by merely inhibiting the absorption of phosphate through some local interaction with the latter in the gastro-intestinal tract.

Almost 30 years ago it was noted that, in rats, certain steroids of the vitamin-D group can produce cardiac necroses with calcification (Selye, 1929a, 1929b). The question now arose whether this type of change could also be influenced by excessive dietary phosphate. Normally, dihydrotachysterol (D.H.T.) produces calcification and necrosis of the cardiac muscle but no inflammatory reaction; however, simultaneous treatment with NaH_2PO_4 transforms the character of these lesions, so that a suppurative acute myocarditis results (Selye, 1958). Like the infarctoid cardiopathy, this inflammatory lesion can be prevented by the concurrent administration of KCl (Selye and Renaud, 1958b).

2. The Steroid Component

Among 34 steroids that have been tested so far, Me-Cl-COL proved to be most effective in producing phosphate-steroid-cardiopathy. However, 2α-methyl-9α-fluorocortisol (Me-F-COL) and the two corresponding non-methylated steroids (9α-chlorocortisol and 9α-fluorocortisol) are likewise very effective in this respect. Among those examined the only halogenated corticoid devoid of this activity is triamcinolone (Δ^1-9α-fluoro-16-hydroxycortisol), a highly active glucocorticoid which possesses little or no mineralocorticoid potency. On the other hand, cortisone, a glucocorticoid with little mineralocorticoid activity, is at least as effective in producing phosphate-steroid-cardiopathy as is desoxycorticosterone, although the latter is much more mineralocorticoid than the former (Selye, 1957d; Selye *et al.*, 1957a). It is especially noteworthy that, when given in combination with NaH_2PO_4, even cortisol (hydrocortisone), the principal natural glucocorticoid of man, can produce such cardiac changes (Selye *et al.*, 1957a; Selye and de Salcedo, 1958); the same is true of the natural corticoid mixture that is secreted by the adrenals of animals treated with large amounts of corticotrophin (Selye *et al.*, 1957a).

Under our experimental conditions, none of these steroids produced cardiac necroses when they were administered without phosphate supplements, and desoxycorticosterone was singularly ineffective in this respect, even when given with NaH_2PO_4. These findings—as well as the relative non-specificity of the protection offered by potassium—make it difficult to evaluate the claim (Darrow and Miller, 1942) that desoxycorticosterone alone (without phosphate) sometimes produces rather similar, though only histologically detectable, cardiac lesions, as a specific result of its hypokalaemic action.

All the steroid hormones that we found to be highly effective in producing the phosphate-steroid-cardiopathy are potent corticoids. However, from the experiments mentioned so far, it was not possible to ascertain whether the cardiotoxic effect is more closely related to the mineralocorticoid or to the glucocorticoid action. Probably both types of activity are important. In experiments in which neither high doses of triamcinolone (a pure glucocorticoid) nor of desoxycorticosterone (a pure mineralocorticoid) produced any marked degree of cardiopathy in NaH_2PO_4-sensitized rats, combined treatment with small doses of both these steroids sufficed to induce pronounced and extensive cardiac necroses (Selye, 1957e). It would appear, therefore, that the concurrent action of mineralocorticoids and glucocorticoids is most effective in conditioning the cardiac muscle to the necrotizing action of phosphates. Of course, the previously mentioned active steroids of the vitamin-D group possess no corticoid actions, but when they are given in combination with phosphates the cardiac lesion that they induce is a suppurating myocarditis, essentially distinct from the infarctoid cardiopathy elicited by steroid hormones under similar conditions (Selye, 1958a; Selye and Renaud, 1958b).

3. The Stress Component

It is important to distinguish between the infarctoid cardiopathy that is produced gradually by the persistent action of phosphates and steroids, and the sudden eliciting effect of stress to which we made only cursory reference in the introductory paragraph. To clarify the specificity of this eliciting mechanism, rats were briefly treated with small amounts of Me-Cl-COL plus phosphate. Although this pretreatment produced little or no cardiac damage, subsequent exposure to the stress of a neuromuscular effort (induced by strapping the rats on to a board) immediately elicited severe and extensive cardiac necroses in 100% of the experimental animals. Indeed, even in rats pretreated only with Me-Cl-COL without phosphate supplements, such neuromuscular exertion occasionally produced cardiac lesions (Selye and Renaud, 1957b).

It might have been thought that neuromuscular exertion acts specifically (not merely through its stressor effect); but in rats similarly sensitized with threshold doses of Me-Cl-COL plus phosphate a high incidence of massive myocardial necroses could also be elicited by bilateral vagotomy, hot or cold baths, multiple bone fractures, crushing of intestines, quadriplegia (subsequent to transection of motor nerves), or toxic doses of adrenaline (Selye *et al.*, 1957b). Although all stressors are not equally effective in this respect, it is evident that the eliciting mechanism is largely non-specific. The possibility of precipitating infarct-like myocardial lesions by sudden exposure to stressors is especially significant, in view of its obvious clinical implications.

It is interesting that, in preparing the heart for the production of acute infarct-like changes by subsequent exposure to a neuromuscular exertion, cortisol is again more effective than desoxycorticosterone (Selye, 1957f).

4. The Question of Species-specificity

The medical implications of all these observations are largely dependent upon the demonstration that the production of such cardiac necroses is not merely a species-specific reaction type peculiar to the rat. It is significant, therefore, that similar cardiac lesions have also been produced by Me-Cl-COL plus NaH_2PO_4 in the guinea-pig, hamster, rabbit, and dog (de Salcedo, 1957; de Salcedo and Selye, 1957). Since the principal glucocorticoid of man is cortisol, it is especially noteworthy that extensive myocardial necroses can likewise be produced in primates (rhesus monkeys) by combined treatment with cortisol acetate and NaH_2PO_4 (Selye and de Salcedo, 1958). This makes it probable that the cardiac muscle of man is also sensitive to this type of action.

5. Relationship to Cardiac Infarcts of Man

Although manifestly similar in their morphological appearance, the lesions of the phosphate-steroid-cardiopathy differ sharply from the true cardiac infarcts of man, in that they cannot be traced to any histologically demonstrable vascular occlusion. Spasms in the larger branches of the coronary arterial system are also unlikely to be involved in the causation of the phosphate-steroid-cardiopathy, because the necroses do not coincide with individual major vascular territories. They may occur in virtually any part of the heart, but we find them most frequently in the thin wall of the right ventricle, as well as in the papillary muscles and the subendocardial layers in both ventricles.

It must be kept in mind, however, that the development of a cardiac infarct depends primarily upon the relationship between the metabolic requirements of the cardiac muscle and its blood supply; hence combined treatment with phosphates and steroids might act by inducing potentially dangerous metabolic changes within the myocardium, so that even physiological variations in the blood supply, which are normally well tolerated, may result in necroses. In this case the precipitating effect of stress could be due either to an additional increase in the demands made upon the cardiac muscle or to temporary variations of the blood supply that are not reflected by any detectable structural change in the coronary vessels. If this concept were correct, the phosphate-steroid-cardiopathy might help to clarify the connexion between those cardiac infarcts of man that are unaccompanied by acute vascular obstructions and the classical infarcts that are due to demonstrable coronary occlusions. All our experiments were performed on healthy young animals with normal cardiac vessels, while spontaneous infarcts tend to occur with the greatest frequency in middle-aged or older men, in whom even a moderate degree of coronary sclerosis may well act as a predisposing factor for metabolic changes similar to those that are induced by combined treatment with phosphates and steroids.

It was thought that in order to elucidate this problem it would be useful, first to produce a moderate amount of coronary sclerosis and hardening (for instance, by pretreatment with D.H.T.), and then to determine whether such an "artificial ageing" of the arterial system can sensitize the heart to the necrotizing effect of subsequent treatment with phosphate and steroid. Over-dosage with a vitamin-D derivative such as D.H.T. tends to cause a rather diffuse sclerosis of the entire coronary system; consequently, if our hypothesis were proved to be correct, it could be expected that after such pretreatment the subsequent administration of phosphate and steroid would affect all parts of the myocardium and would not be restricted to the usual sites of predilection for the localization of the phosphate-steroid-cardiopathy. It is the object of this communication to report upon experiments in which this hypothesis has been verified.

Materials and Methods

Thirty female Sprague-Dawley rats, with a mean initial body weight of 103 g. (range, 98–109 g.), were subdivided into three equal groups and treated as indicated in the accompanying Table. During the first 10 days (the "pretreatment period") D.H.T. was given to groups II and III, in the form of a microcrystal suspension, at the dose of 300 μg. in 0.5 ml. of water once daily, by stomach tube. The rats of group I, which were to act as controls, received no such pretreatment. Then followed a rest period of 10 days, during which no treatment was given to any of the groups, but the food intake of the rats in group I was reduced, so as to bring their body weight close to that of the animals in groups II and III, whose growth rate was reduced by the D.H.T. pretreatment. Beginning on the 20th day of the experiment (that is, after 10 days' rest), the rats of groups I and II received 50 μg. of 2α-methyl-9α-chlorocortisol (Me-Cl-COL), in the form of microcrystals of its acetate, in 0.2 ml. of water once daily, subcutaneously, and 300 mg. of monosodium phosphate ($NaH_2PO_4.H_2O$), in 2 ml. of water twice daily, by gavage, until termination of the experiment. During this period the rats of group III were untreated.

Throughout the experiment the animals received only the normal laboratory diet: "Purina Fox Chow" and tap-water. On the 30th day the experiment was terminated by killing all survivors with chloroform. The hearts and kidneys were fixed in neutral formalin for subsequent staining with hematoxylin-phloxine (to show general structure) and with von Kossa's silver nitrate technique (for the histochemical demonstration of calcium).

The mortality rate, the mean body weight just before and after Me-Cl-COL plus NaH_2PO_4 treatment, as well as the mean intensity of myocardial necrosis, coronary calcification, and coronary obstruction (all arbitrarily graded 0 to 3) are listed with their standard errors in the Table.

Results

After five to six days of NaH_2PO_4 plus Me-Cl-COL treatment, all the rats of group II (pretreated with D.H.T.) became manifestly ill, and 80% of them died with multiple yellowish myocardial foci which were clearly visible on naked-eye inspection.

Upon histological examination, only occasional small spots of myocardial necrosis (some with secondary invasion by histiocytes and a few polymorphonuclear cells) were seen in *group I*. These foci were predominantly localized throughout the substance of the thin wall of the right ventricle, as well as in the papillary muscles and subendocardial strata of both ventricles—that is, in locations typical for the infarctoid cardiopathy. In none of the animals of this group were there any detectable morphological changes in the coronary vessels.

The picture was entirely different in the rats of *group II* which received the same Me-Cl-COL plus NaH_2PO_4 treatment but were pretreated with D.H.T. Here myocardial necroses were much more extensive and quite irregularly

Humoral Production of Cardiac Infarcts

Group	Pretreatment	Body Weight before Treatment (g.)	Treatment	Body Weight after Treatment (g.)	Cardiac Lesions (Scale: 0–3)			Mortality (%)
					Myocardial Necrosis	Coronary Calcification	Coronary Obstruction	
I	None	133 ± 1·5	Me-Cl-COL + NaH_2PO_4	150 ± 2·1	0·9 ± 0·25	0	0	0
II	D.H.T.	126 ± 3·3	Me-Cl-COL + NaH_2PO_4	127 ± 2·4	2·9 ± 0·2	2·3 ± 0·28	2·1 ± 0·2	80
III	D.H.T.	132 ± 3·8	None	160 ± 3·8	0	0·6 ± 0·14	0·8 ± 0·14	0

distributed throughout the myocardium (Figs. 1 and 2). In addition there was intense calcification in virtually all the ramifications of the coronary arterial system. The calcium deposits took the shape of irregularly fragmented blocks which, in many places, appeared to break through the intima into the vascular lumen and also extended into the adventitia. In contact with these calcified masses there was often connective-tissue proliferation; occasionally inflammation and thrombosis were present. In many arteries there developed an intense subintimal oedema, which led to a considerable reduction or virtual obliteration of the vascular lumen (Fig. 3). Such changes are rather reminiscent of the lesions described by Müller (1949), Bredt (1949), Büchner (1955), and others as being characteristic of the acute coronary death that occasionally occurs in young men, especially in soldiers exposed to the stress of battle.

FIG. 1.—Macroscopic appearance of the heart of a rat of group III merely pretreated with D.H.T. (left) in comparison with that of an animal from group II which, after D.H.T.-pretreatment, received Me-Cl-COL plus NaH_2PO_4. Note the absence of macroscopically visible changes in the former, while in the latter there are large, irregular light infarcts scattered throughout the substance of both ventricles.

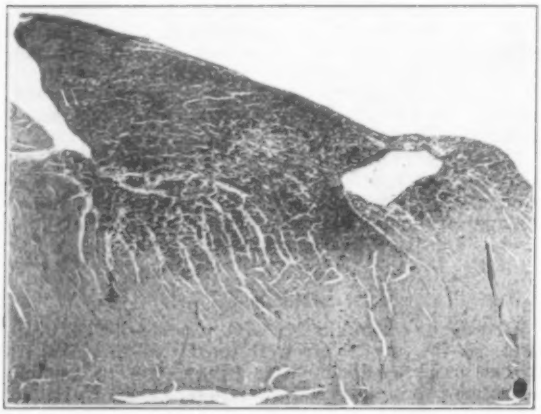

FIG. 2.—Large infarct involving a whole papillary muscle in the left ventricle of a rat from group II. (Haematoxylin-phloxine. ×15.)

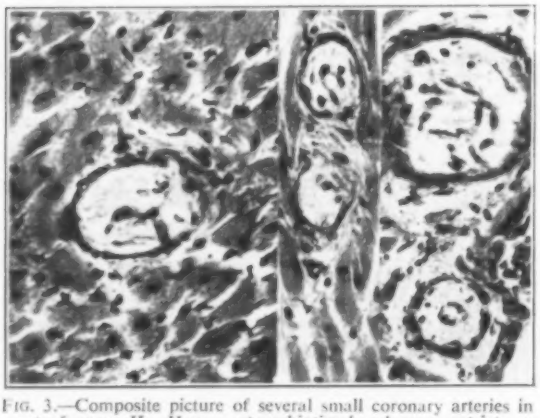

FIG. 3.—Composite picture of several small coronary arteries in a rat of group II. Here, acute subintimal oedema constricts or obliterates the lumen. (Haematoxylin-phloxine. ×230.)

As a result of all these changes the lumen of the entire coronary system, from the largest to the smallest arterial vessels, became greatly narrowed, and in some places it was completely obstructed (Fig. 4). In many large or medium-sized arteries where the obliteration was only subtotal—one or two capillary-sized channels still permitting the passage of blood—it was difficult to differentiate between an excessive acute intima proliferation and the recanalization of an organized thrombus (Fig. 5). In any event, in the coronary system of all the animals in group II (including the two that survived until termination of the experiment) severe mechanical interference with the coronary circulation was quite obvious.

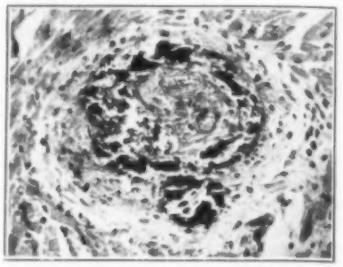

FIG. 4.—Numerous fragmented calcium deposits in the wall, with complete obliteration of the lumen of a coronary artery of a rat from group II. (von Kossa's stain. ×150.)

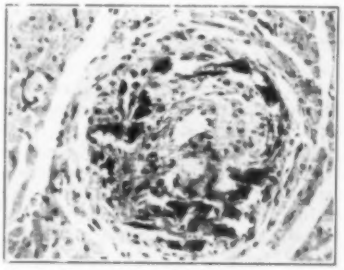

FIG. 5.—Subtotal obliteration of the lumen of another coronary artery from the heart shown in Fig. 4. (von Kossa's stain. ×150.)

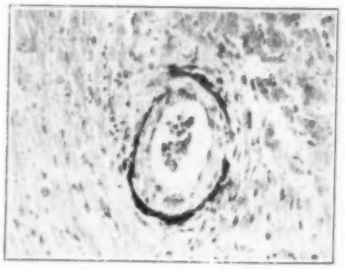

FIG. 6.—One of the most intensely calcified arteries of an animal from group III. Here the calcium deposition is regular (not fragmented) and limited to the media. The intima is moderately thickened, but the lumen remains widely patent and the endothelium intact. (von Kossa's stain. ×150.)

In contrast, the rats of *group III*—that had been similarly pretreated with D.H.T., but received no subsequent treatment with Me-Cl-COL plus NaH_2PO_4—revealed only a moderate degree of calcium deposition in the media (Mönckeberg type), limited to a few of the coronary arteries. Even in the most seriously affected vessels (Fig. 6) the calcium deposits formed only thin regular (not fragmented) plaques, which evoked no proliferative reactions in the surrounding tissue, except for occasional slight thickenings in the adjacent intima. Severe obstructions of coronary vessels could not be found in any of the animals of this group.

Discussion

The typical coronary lesion that usually predisposes for the development of cardiac infarcts in man is an atheromatosis, primarily characterized by lipid deposition and intima proliferation with comparatively little calcification. In our experiments, on the other hand, the D.H.T. pretreatment caused mainly calcium deposition, with little intima proliferation and virtually no lipid deposition. However, in both cases the mechanical effect of the morbid lesions is essentially the same: some degree of constriction and considerable rigidity of the arterial wall. It will be recalled that our object in carrying out these experiments was to verify whether an artificially produced vascular change of this kind would predispose the cardiac muscle to the necrotizing action of subsequent treatment with Me-Cl-COL plus NaH_2PO_4. The data presented here show that this was the case. It remains to be established whether interference with the coronary circulation, no matter how produced, would exert a similar sensitizing effect. However, the present experimental series justifies the conclusion that short-term treatment with D.H.T. can so stigmatize the heart that even after clinical recovery the animals remain sensitized to such metabolic derangements as are induced by the subsequent administration of Me-Cl-COL plus NaH_2PO_4. In a sense, this stigmatization may perhaps be compared with the effects of ageing and the associated atheromatosis in the human coronary circulation.

Although we suspected that the coronary damage produced by D.H.T. could thus predispose the cardiac muscle to the necrotizing effect of Me-Cl-COL plus NaH_2PO_4, it was not expected that the latter treatment would also aggravate the arteriosclerosis itself. It is noteworthy, however, that, under these circumstances, not only cardiac infarction but organic obstruction of the coronary vessels can regularly be produced by humoral means.

Further experiments will have to show whether there is any close relationship between this experimental disease and the spontaneous coronary infarcts of man. It also remains to be seen whether the magnesium and potassium salts that proved to be so eminently effective in the prophylaxis of the phosphate-steroid-cardiopathy will also prevent those types of cardiac necroses that are associated with vascular obstructions.

Summary

Based on the literature concerning the infarct-like cardiac necroses that are produced by combined treatment with phosphates and steroids (the "phosphate-steroid-cardiopathy"), experiments were designed to determine whether a pre-existent coronary lesion would sensitize the cardiac muscle to this type of damage.

Albino rats were pretreated during 10 days with dihydrotachysterol (D.H.T.), so as to produce mild narrowing and calcification of the coronary arteries. After this, no further treatment was given until all the animals had recovered, as judged by their growth and clinical appearance. Then, combined treatment with NaH_2PO_4 plus 2α-methyl-9α-chlorocortisol (Me-Cl-COL) was initiated at a dose level which in non-pretreated animals caused only occasional microscopical foci of myocardial necrosis, localized in certain areas of predilection. It was found that in the D.H.T.-pretreated rat this same NaH_2PO_4 plus Me-Cl-COL treatment produces extensive macroscopically visible patches of necrosis throughout the myocardium and, at the same time, evokes intense, proliferative, and eventually obstructive changes in all parts of the coronary tree.

The possible relationship between this type of experimental disease and the spontaneous coronary infarcts of man is discussed.

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TREATMENT OF APHTHOUS ULCERATION OF THE MOUTH

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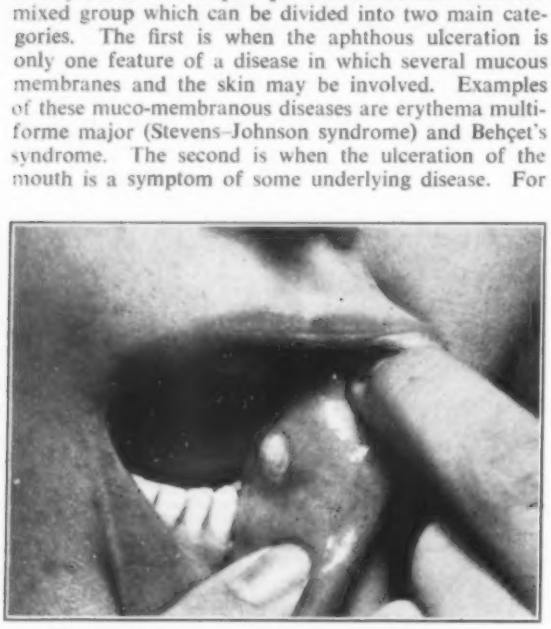
(From the Radcliffe Infirmary, Oxford)

Aphthous ulceration of the mouth is one of the commonest minor maladies. It is probable that within the British Isles more than a million persons are affected with the condition. In its common or *minor* form a single ulcer or a small crop of ulcers appears on the buccal mucous membrane several times a year. The ulcers occur most often on the inside of the cheeks (see illustration) opposite the molar teeth, inside the lips, and occasionally on the tongue, although any part of the mouth or pharynx may be affected. They are painful and interfere with speech and eating, but normally they run a short course and heal in about a week without scarring.

Some patients suffer from a *major* form of aphthous ulceration, which is a much more severe condition. The ulcers are multiple and the patient may be seldom, if ever, free from them over the course of years. When this is so, the disorder ceases to be merely a painful inconvenience and assumes the dimensions of incapacitating illness. Patients thus afflicted with the major form of the condition are fortunately a small minority of the total, but they are nevertheless numerous within the general population.

There is a *special* group of patients showing ulceration of the mouth which is, at any rate superficially,

closely similar to simple aphthous ulceration. This is a mixed group which can be divided into two main categories. The first is when the aphthous ulceration is only one feature of a disease in which several mucous membranes and the skin may be involved. Examples of these muco-membranous diseases are erythema multiforme major (Stevens–Johnson syndrome) and Behçet's syndrome. The second is when the ulceration of the mouth is a symptom of some underlying disease. For



Photograph showing aphthous ulcer inside the cheek.

example, in tropical sprue and idiopathic steatorrhoea, aphthous stomatitis is extremely common; indeed, the term *sprue* is derived from the Dutch word *spruw*, which means aphthous disease (Dubois and van den Berghe, 1948). In ulcerative colitis, aphthae occur fairly often during the stage of symptoms.

Aetiology

The aetiology of aphthous ulceration is essentially unknown, though many theories have been advanced, the most popular being that the ulcers are psychosomatic or allergic manifestations or that they are caused by a virus. Treatment is therefore empirical and has remained unsatisfactory. Simple mouth-washes and paints have little influence on the course of the ulcers. Various vitamins have been used, but without convincing evidence of success. The ulcers can be cauterized by touching them with a silver nitrate stick or with chromic acid solution, but such violent methods can only be deplored, because they enlarge the ulcers and are likely to give rise to residual scarring.

The situation has been summed up admirably by Erich (1955) in a celebrated textbook of medicine when he says: "There is no known cause for aphthous stomatitis and there is no treatment which is of any value." This discouraging comment is reinforced by the findings of Sircus *et al.* (1957) in a recent study of 120 patients suffering from the disorder. They carried out blind controlled trials of many of the most popular treatments, and found none that would reduce the chance of ulceration occurring. The agents thus found to be useless were: folic acid, nicotinamide, riboflavine, a vitamin-B mixture, small doses of cortisone by mouth, ethisterone for premenstrual aphthae, and local radiotherapy. Their one positive finding was that the local application of chlortetracycline appeared to speed up the healing of the ulcers although it did not prevent them from recurring.

Treatment

In view of the fact that cortisone and its analogues have been found useful in the treatment of inflammatory conditions when they are applied locally, it is natural to wonder whether these compounds have any useful place in the treatment of aphthous ulceration. Fisher (1955) treated eight patients who suffered from recurrent aphthae with hydrocortisone ointment, but did not find it very helpful, as five obtained no relief whatever. Rivin and Barton (1955) made a "blind" controlled study of the effect of hydrocortisone ointment and found no effect on the time of healing, although a few patients experienced relief of pain. However, Hillman (1956) and Morton (1957) claimed good results from treating aphthous ulcers by the direct application of hydrocortisone ointment. It is evident that no agreement has yet been reached on whether hydrocortisone ointment is of any great value in the treatment of the condition.

The mouth is far from being a suitable place for the use of an ointment for local therapy. The whole surface is bathed in saliva, which must impede the action of a substance carried in an ointment. The movements of the tongue and cheeks make it improbable that an ointment will stay long in place on any localized lesion within the mouth. It occurred to us to make a virtue out of necessity by using a water-soluble compound of hydrocortisone which would dissolve in the saliva. Instead of being an inconvenient barrier, the saliva then becomes the actual solvent for the hydrocortisone and the medium by which it is transported to the lesion. At our request Glaxo Laboratories prepared a tablet especially for use in the mouth; it contained 2.5 mg. of hydrocortisone in the form of its hemisuccinate sodium salt, a compound freely soluble in water and one which has proved to be beneficial in the local treatment of ulcerative colitis (Truelove, 1957). The tablets have a lactose base and are designed so that they will dissolve slowly.

We have treated 52 patients suffering from aphthous ulceration with these tablets. The results have been highly favourable, and we now report them with brief illustrative case histories.

Minor Form of Aphthous Ulceration

In 23 patients with the minor form we have found it sufficient to wait for the appearance of an ulcer and to apply treatment by placing one tablet in the mouth in close proximity to the ulcer and leaving it to dissolve. This takes about three-quarters of an hour. It is usual for the pain of the ulcer to be relieved by the time the tablet has dissolved. This is repeated up to four times a day until the ulcer disappears. With this treatment a fully established ulcer will usually heal in 36 to 48 hours. When the treatment is used with an ulcer in the earliest phase of development—that is, when its diameter is only 1–2 mm.—the ulcer does not develop but remains small, and is commonly gone by the next day. Typical examples are given.

Case 1.—A schoolgirl aged 16 (the daughter of one of us) for several years had suffered from aphthous ulcers which occurred every few weeks. In June, 1957, she had an unusually severe ulcer which was very painful. When it was fully developed, a tablet was placed in the mouth in contact with it. The next morning, when asked how the ulcer was, she replied, "Oh, I had forgotten all about it." Examination then revealed the ulcer to be still present, but it appeared to be in a healing phase, and without further treatment had gone by the next day, being painless throughout. Since that episode she has had four aphthous ulcers, but each time the ulcer has been treated during its early stages while it was still very small. On no occasion did the ulcer develop into its usual full size. On three occasions it had disappeared by the next day, and on the fourth in 48 hours. A conspicuous feature has been the prompt relief of pain, so that after the use of a tablet the tongue can be rubbed vigorously over the ulcer without causing discomfort.

Case 2.—A schoolboy aged 13 (the son of one of us) had been subject to aphthous ulcers for several years, though they came at less frequent intervals than in Case 1. During the period of our study he has had three aphthous ulcers, and on each occasion, following treatment with one or two tablets, the ulcer has failed to develop and has gone by the next day. The relief of pain is rapid after the use of the first tablet.

Case 3.—A medical specialist aged 33 had suffered from recurrent aphthous ulceration since the age of 12 years. Ulcers came at irregular intervals, sometimes singly and sometimes in crops. They persisted with pain for 7 to 10 days. On September

18, 1957, he was conscious of soreness inside the right cheek, and by the next day a definite ulcer had appeared. That evening he applied two tablets at an interval of two hours. The next morning he was free of pain, but the ulcer was still present and there was some pain by the evening. A third tablet was then used and thereafter there was no pain and the ulcer disappeared. In his own words, "cure in 36 hours." A few weeks later another aphthous ulcer occurred. One tablet gave rapid and complete relief of pain, which was followed by healing within 48 hours without further treatment.

The other 20 cases of minor aphthous ulceration have, with one exception, responded similarly to the three described above. This was a general practitioner aged 31 who had suffered from aphthous ulcers for a number of years and was accustomed to treat them by the application of a silver nitrate stick. This would cause severe immediate pain; but the pain would soon go, although the ulcer would persist for a week or 10 days. In October, 1957, he developed a streptococcal sore throat with fever and malaise, and three days later three large aphthous ulcers occurred. He treated these by his usual method of cauterization, but on this occasion failed to obtain relief. At this stage he tried treatment with the hydrocortisone mouth tablets, but these were totally ineffective. We do not regard this as being a straightforward case of failure, because the lesions had already been transformed from aphthous ulcers into chemical burns. He has not yet had a recurrence, so that there has been no opportunity for treatment of a primary lesion.

Major Form of Aphthous Ulceration

In 22 cases of the major form we have found it best to begin treatment with one tablet four times day and to continue at this level until ulceration has ceased. All patients have made a good initial response.

Thereafter we have continued a regular maintenance use of the hydrocortisone tablet in an attempt to prevent or abort further ulceration. In some patients two tablets a day have been sufficient for maintenance therapy, but others have been left on the full dose of four tablets a day. Five patients have remained completely free of ulceration for some months on this regime. Most of the others have continued to get sporadic sore spots in the mouth, but without ulceration, so that their actual disability has ceased. Some others, although greatly improved, have continued to develop occasional single ulcers while under treatment. One patient (Case IV) has shown evidence of temporary relapse during treatment. Illustrative examples follow.

Case I.—A senior Government official aged 46 had suffered from almost continuous aphthous ulceration since early childhood. He would have two or three ulcers at a time, and as one crop healed another developed. He was never free for more than a week or two. He had consulted many doctors and had received numerous treatments, none with any great effect. When first seen by us he had ulcers on the right cheek and soft palate, and extensive areas of intense erythema which were sore to contact. He became free of symptoms within two days of starting treatment with the tablets, and when examined two weeks later the mouth was normal. He then went on to maintenance treatment with two tablets a day and has remained normal during the succeeding six months. During this period of freedom from symptoms he was undergoing considerable mental strain through personal friction at his work, which is interesting because of a prevalent view that mental stress causes aphthous ulceration.

Case II.—A typist aged 22 had suffered from the minor variety of aphthous ulceration in childhood, but at the age of 14 the ulceration became more frequent and more severe. Since that time she has seldom been free from multiple ulcers for longer than a fortnight, and often suffers from them continuously for three or four months at a time. When first seen by us she had three large ulcers and several small ones. Three days after starting treatment she was improving, and after the first week only the healing residue of the largest ulcer was left. She continued on the full dose of four tablets a day for a further three weeks without ulceration, and was then put on to two tablets a day. On this dose occasional tiny tender spots developed in her mouth which did not ulcerate and which disappeared in two to three days. Pain was negligible, whereas previously she had found eating and speaking an ordeal.

Case III.—A housewife aged 33 had suffered from severe aphthous ulceration with every menstrual period since the age of 18. Six days before the beginning of menstruation numerous aphthous ulcers would develop, scattered all over the mouth. They grew and were very painful until the actual onset of menstruation, and then healed during the next six days. If the menstrual period came early the ulcers also came early, preserving the exact time relationship. We gave her intermittent treatment timed to precede the expected outbreaks. On each successive occasion numerous tiny ulcers developed; these never increased in size, although they persisted for several days. They were painful when she awoke in the morning, but the pain disappeared while she was using the first tablet of the day and was not felt again until the following morning. On one occasion when there were 25 of these tiny ulcers inside the upper lip she demonstrated to us that she could rub the tongue vigorously over them without pain.

Case IV.—A female factory hand aged 30 had suffered from severe aphthous ulceration since her earliest recollection. She had never been free of ulcers at any time and usually there were at least six. When first seen by us several ulcers were present. During the first week of treatment she improved, but tiny ulcers continued to appear, and during the next fortnight two ulcers developed which healed quickly. During the fourth week of treatment she was free of ulcers for the first time in her memory. In the second month of treatment she had one ulcer following influenza, but it remained small and healed in four days. In the third month there was recurrence of ulceration with a crop of ulcers in the mouth, of which one was still present when we saw her. With further treatment she has again become free of ulcers.

Aphthous Ulceration as Part of a Mucomembranous Disease

In the few examples of this which we have had an opportunity to treat, the aphthous ulceration has shown the same response to treatment as simple aphthous ulceration.

Behçet's Syndrome

There were three probable cases of this syndrome, which in its complete form consists of recurrent oral and genital ulceration, with associated eye lesions, especially iritis (Phillips and Scott, 1955). It is often known as the triple symptom-complex of Behçet, who first described it as a distinctive syndrome (Behçet, 1937). It is a generalized disorder, and various systemic manifestations may occur in addition to the local changes already mentioned (France *et al.*, 1951). Neurological complications may occasionally arise because of widespread vascular lesions. The syndrome is often incomplete, with only two, or even one, of the mucous membranes affected.

Case A.—A housewife aged 64 had suffered from aphthous ulceration for 12 years. For the first 10 years she had attacks of ulceration every few months associated with epigastric pain and a retrosternal burning sensation, together with anorexia and a furred tongue. Each attack lasted about a month. Then, following the accidental death of her son, the aphthous ulceration became almost continuous and very severe, while the associated symptoms also continued. Ulcers were apt to affect the pharynx as well as all parts of the mouth. At the same time she developed severe pruritus ani and vulvae, which were treated with hydrocortisone ointment with benefit. When first seen by us she had two ulcers on the soft palate. There was also mild conjunctivitis. The E.S.R. was raised, being 31 mm. in one hour (Westergren) and it has remained at this level since. On two tablets a day for two months she was free of ulcers in the mouth proper, but continued to get ulcers about the fauces and in the pharynx. Judging that the mouth tablets were not a satisfactory means of getting a sufficient concentration of hydrocortisone to the pharynx, we then put her on a gargle of hydrocortisone (free alcohol) made up by diluting 50 ml. of the alcoholic solution (containing 250 mg of hydrocortisone) with 500 ml. of normal saline. This was gargled several times a day for as long as was practicable on each occasion and then spat out. This treatment relieved the ulceration of the pharynx and fauces. We next instructed her to return to the use of the hemisuccinate tablets, but to hold saliva in the mouth until there was sufficient accumulated to permit it to be used as a gargle. This method has proved as effective as the use of a gargle prepared along more conventional lines.

Comment.—The occurrence of pruritus ani and vulvae, the mild conjunctivitis, the severe retrosternal burning sensation and epigastric pain, and the persistently raised E.S.R. make

us regard this patient as an example of Behçet's syndrome. Such patients benefit from cortisone and its analogues used systemically, but we have not so far made use of this form of treatment.

Erythema Multiforme Major (Stevens-Johnson Syndrome)

There was one case of this illness. In its complete form this syndrome manifests itself as erythema multiforme, ulceration of the mouth, urethritis, and conjunctivitis, but incomplete forms often occur. It is an acute disease, usually self-limited, and clearing up in six to eight weeks.

Case B.—Apart from one isolated crop of aphthous ulcers 14 years previously, a children's nurse aged 36 had had no mouth lesions until October, 1957, when she developed herpes labialis at the same time as the children under her care had influenza. A few days later a bullous eruption appeared on the backs of both hands and in front of both knees and lower legs. A day or two later severe ulceration of the mouth occurred, together with much malaise and a low-grade fever. Her family doctor described the mouth as "the worst I have ever seen, with large, deep, excoriated ulcers on the insides of her cheeks and the sides of her tongue, while the tip of the tongue was raw." This clinical picture persisted for a month, when the skin lesions died down and she became well in herself but repeated crops of aphthous ulcers continued. When we saw her at this stage there were two active ulcers inside the lower lip with hyperaemic and oedematous zones surrounding them and patches of hyperaemia and superficial scarring elsewhere in the mouth. Pigmented areas 1 to 2 cm. in diameter were present on the skin at the site of the original eruption. Treatment with mouth tablets relieved her of all pain and soreness in two days, and there has been no further ulceration.

Comment.—The disease being self-limited, the tablets were used only at the tail-end of the attack, and we have not had the opportunity of testing their action at the height of an attack.

Aphthous Ulceration in Association with Some Underlying Disease

Idiopathic Steatorrhoea (1 Case)

Both in tropical sprue and in idiopathic steatorrhoea, aphthous ulceration is very common. In idiopathic steatorrhoea Cooke *et al.* (1953) found that 90% of patients suffered from the ulceration.

Case C.—A housewife aged 24 had been diagnosed as suffering from coeliac disease as a child. Her development was slow, with the menarche at the age of 18. For some years her bowel habit had been normal, but she had been on a gluten-free diet for two or three years. For the whole of her life she had been subject to recurrent aphthous ulceration, which was of a "minor" character until two years previously, when she came to Oxford and abandoned the gluten-free diet. Since that time she had had increasingly severe ulceration, which was almost continuous during the six months previous to seeing us. She could not eat without pain and could not enjoy a cigarette. When we first saw her there were extensive areas of hyperaemia of the buccal mucosa with frank ulceration at six places. Use of the tablets in a full dose of four a day made the mouth normal. She then went on to a maintenance dose of two tablets a day. With this level of dosage there was no ulceration, but occasional small red tender areas appeared on the buccal mucosa and lasted for a few days.

Comment.—It has already been mentioned that this patient had no bowel symptoms. A radiological survey of the skeleton by Dr. F. H. Kemp revealed normal maturation and no evidence of osteomalacia. Her stature was that of a small normal woman. Her fertility was normal, as she conceived quickly after marriage and gave birth to a healthy baby. Blood examination revealed a persistent mild hypochromic anaemia with anisocytosis and polychromasia of the red cells. We have little doubt that the coeliac disease has persisted as idiopathic steatorrhoea, even though her domestic obligations have made it inconvenient for her to enter hospital for a study of the fat balance. It is now known that coeliac disease persists into adult life (Lindsay *et al.*, 1956), and that adult patients with idiopathic steatorrhoea have commonly suffered from symptoms in childhood. Both are due to sensitivity to gluten in wheat and rye, and a lifelong diet which excludes this appears to be advisable (French *et al.*, 1957). We have now put this patient on to a gluten-free diet, but we regard the fact that the aphthous ulceration responded well to the mouth tablets in the absence of any dietary treatment as a matter of interest.

Ulcerative Colitis

In this disease, of which there were two cases, aphthous ulceration of the mouth not infrequently accompanies the stage of bowel symptoms. In both cases the mouth ulceration has responded swiftly to the use of the mouth tablets.

Discussion

The method of treatment which we have described is not only effective in the great majority of patients but is also simple and safe. A tablet is easily held in the mouth and will rest in the gingival sulcus, where aphthous ulcers most commonly occur. Its slow dissolution ensures that the ulcer is bathed in saliva charged with hydrocortisone for a rather long period. A certain amount of trouble must be taken to obtain contact between the tablet and the ulcer in patients with ulceration of the tongue or palate. So far as safety is concerned, our maximum dose has been four tablets a day, which represents 10 mg. of hydrocortisone, a dose unlikely to have any harmful systemic effect, however long continued.

When ulceration is present the tablets must be kept in close relationship to the ulcer if they are to be effective. When the tablets are being used as maintenance treatment to prevent ulceration, we have advised patients to shift them about the mouth every few minutes in order to carry the hydrocortisone to all parts of the buccal mucosa.

There has been a tendency to combine hydrocortisone with antibiotics for local application. We have not used antibiotics for treating aphthous ulcers, for two reasons—they are unnecessary and are potentially dangerous. Hydrocortisone has emerged as a satisfactory treatment when used alone by the method described. Antibiotics are known to carry the risks of sensitizing mucous membranes and of encouraging fungal growth; their use on mucous surfaces for indefinite periods therefore demands caution. In any event, there is no evidence that simple aphthous ulceration is an infective condition. Although it has often been thought to be herpes simplex affecting the buccal mucosa, this idea has been refuted by many studies, of which a particularly good one is that by Stark *et al.* (1954).

It is not our purpose here to deal generally with the aetiology of aphthous ulceration, but there is one aspect to which we should like to draw attention. It has commonly been supposed that mental stress is an important causative factor, a view advanced in the first British description, which bore the title of "Neurotic Ulcers of the Mouth" (Sibley, 1899). We ourselves have been more impressed by the mental disturbance created by the major form of aphthous ulceration and by the improvement in mental well-being when treatment is effective. For example, the father of our Case II, a superintendent of police, spontaneously told us of the great improvement in their home life since his daughter obtained relief from almost continuous oral pain. In another of our major cases (not one of those reported in detail) the patient described how he had become silent and morose because of the pain it gave him to talk, whereas after treatment he took delight in being normally sociable.

Summary

A method of treatment of aphthous ulceration of the mouth is described using a water-soluble compound of hydrocortisone incorporated in tablets which dissolve slowly in the mouth. The saliva then acts as the medium of transport to the mucosal surface.

Treatment has been given to 52 patients, of whom 23 were examples of the common or minor form of the condition, 22 were examples of the major form, and 7 were special cases of muco-membranous disease or of aphthous ulceration complicating another disease.

With one exception, the minor cases have obtained rapid relief of pain and healing of the ulcer has been accelerated.

The major cases have generally derived great benefit from the treatment. All showed initial improvement. With maintenance treatment some have been completely free of ulceration during several months of observations. Others have had minor ulceration but are greatly improved. Only one has shown a tendency to relapse during treatment.

The special cases have likewise shown a good response.

We are indebted to Glaxo Laboratories, who not only made the hydrocortisone hemisuccinate tablets specially for this study but also supplied them as a gift.

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SPREAD OF STAPHYLOCOCCI IN A SURGICAL WARD

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In the summer of 1956 a surgical unit at St. Bartholomew's Hospital suffered a severe outbreak of staphylococcal infection in which staphylococci of a single phage type caused 31 infections in two months. The staphylococcus appeared to be spread in part by a member of the surgical team who was a carrier, but there was also evidence of spread within the ward (Shooter, Griffiths, Cook, and Williams, 1957). The large number of staphylococci found in the air and on the bedclothes in the ward raised the question of the importance of air-borne transfer in the spread of infection within the ward, and of the value of measuring air and dust contamination with staphylococci in the prediction of outbreaks of infection.

The male ward of the unit was redecorated in September, 1956, and the opportunity was thus presented of observing the recolonization of a clean ward by staphylococci, and possibly of tracing the source of staphylococci isolated from the air and from objects in the ward.

This study of the natural history of *Staphylococcus aureus* had not proceeded far when we observed the first example of the wide dissemination of a single phage type of staphylococcus, without, however, the occurrence of any wound sepsis. The study continued for eight months (until May 31, 1957), during which we observed nine waves of staphylococcal "broadcast," in each of which the numbers of staphylococci of one phage type reached an unusually high level (0.1 bacteria-carrying particle per cu. ft. (3.5 particles per cubic metre) of air) and, in most cases, comprised 60–80% of the staphylococci found in the air at the time. Of the nine staphylococcal broadcasts, only three were associated with clinical infection in more than one patient. These observations lend colour to the idea that some staphylococci are less virulent than others, and also that some patients shed staphylococci more freely than their neighbours.

In this paper we record, first, the extent to which patients acquired staphylococcal infection of wounds and other parts, and to which patients and nurses became nasal carriers during their stay in the ward. We also describe the extent of staphylococcal contamination of inanimate objects—particularly bedclothes and bed-curtains—and the air. Second, we describe the staphylococcal broadcasts and discuss their probable genesis and observed effect.

By means of phage-typing it is now possible to recognize many separate and distinct types of *Staph. aureus* that are ordinarily quite stable. With an organism as common as *Staph. aureus* some typing method of this sort is essential for a study of the epidemiology of infections. The usefulness of the method is emphasized by the fact that some 186 apparently distinct types of staphylococci were recognized during our eight months' study.

A possible source of confusion was introduced into our investigation of the spread of infection by the decision, prompted by experience in the summer outbreak, to isolate in a side-room any patients infected with staphylococci thought to be particularly virulent, which in the event proved to be those resistant to both penicillin and tetracycline.

The Investigation

The study was made in a male surgical ward. The work of the unit consisted of general surgery with a considerable proportion of abdominal and rectal operations. The ward had 22 beds, spaced about 6 ft. (1.8 m.) apart, with three more beds in two side-rooms. There were cotton curtains, suspended from rails 7 ft. (2.1 m.) high, that could be pulled out to surround each bed. Wound dressings were done in the ward by a no-touch technique. Patients infected with what were thought to be dangerous staphylococci were nursed in one of the two side-rooms. Special nurses were not employed, but a strict barrier-nursing routine, including the wearing of gowns, was followed.

A variety of minor steps were taken which it was hoped would help to check the spread of staphylococci. All the bedding from the patients who were nursed in isolation was disinfected with formaldehyde before being sent to the laundry. Curtains in the ward were changed once every four to five weeks. The floors were

wax-polished and swept with a vacuum cleaner. No dressing cloths were used on the top of dressing trolleys, which were wiped with 0.2% sodium hypochlorite solution between each dressing. Hypochlorite was also used for disinfecting the bath after each patient, for the urinals, for wash-basins, and for lavatory seats, which were wiped three times a day instead of being polished. Soiled dressings were put immediately into a bin with a pedal-operated lid, and the unused contents of sterile opened dressing packets were put to one side for resterilization. In a previous study staphylococci had been isolated from unused materials (and from a dressing-trolley cloth) at the end of a dressing, and if not removed there was a temptation to use the lately sterile dressings for miscellaneous tasks. For a similar reason cloth urinal covers were replaced by disposable paper covers.

Bacteriological Methods

Swabs were taken from wounds routinely at first dressing and subsequently if infection was suspected on clinical grounds. Specimens of sputum and urine were examined as thought necessary. Nasal swabs were taken from the medical and nursing staff and the ward cleaners and kitchen staff weekly, and from patients on admission and weekly thereafter.

On week-days during the first three and a half months of the study samples were taken from bedclothes, bed-curtains, dressing-trolley tops, baths, basins, lavatories, etc., a total of 877 examinations being made. The sweep-plate method (see Blowers and Wallace, 1955) was used for fabrics; swabs were used for other objects. Air was examined with a slit sampler on one day in each week: on average about 180 cu. ft. (5.1 cubic metres) was sampled. During May a new slit-sampler was introduced and it was possible to take air samples daily; the total volume examined each week was 150–240 cu. ft. (4.25–6.8 cubic metres).

Blood agar was used for the cultivation of specimens from persons and articles; for the air samples we employed serum agar containing phenolphthalein phosphate (Barber and Kuper, 1951) as an indicator medium.

From all cultures, colonies resembling *Staph. aureus* were tested for coagulase, and coagulase-positive strains were submitted for phage-typing. Strains from people and objects in the ward were also tested for antibiotic sensitivity.

Staphylococci were tested for phage sensitivity and classified into a number of types by means of the methods and rules already described (Williams and Rippon, 1952; Anderson and Williams, 1956). The "types" quoted are lists of the phages to which the strain was sensitive; types that could be determined only with strong phage filtrates are printed in italic. The suffix "w" indicates weak reactions, and "+" indicates additional minor reactions.

Some 15 types were each isolated from many different sources; these types were reasonably well defined and distinguished from each other, and from other strains encountered. There were a great many other phage patterns that were seen only once or on a few occasions; with these it is less easy to be sure how many distinct types were present, but we estimate that there were at least 186.

Records.—In addition to conventional records and a wound-book for recording the state of operation wounds (see Shooter, Taylor, Ellis, and Ross, 1956) a record was made each day of the position of patients' beds in the ward, of operations and wound dressings, and of what was known of the distribution of staphylococci.

Chemotherapy.—Of the 311 patients admitted to the ward during the period of this investigation, 128 received one or more antibiotics, but no routine pre-operative chemotherapy was given, except for operations on the small and large intestine. Of the 128 patients, 82 were given sulphonamides, 78 penicillin, 17 streptomycin (usually by mouth), 8 neomycin (by mouth), 5 erythromycin, and 3 tetracycline; novobiocin and E.129 for two patients, and nitrofurantoin ("furadantin") and nystatin each for one patient.

Results

Staphylococcal Infection of Clean Wounds

During the study 311 patients were admitted to the ward, and 195 underwent operations involving cutting skin or mucosa; many of these operations were on the gastro-intestinal tract. Sixteen operations were into infected regions: these comprised 11 haemorrhoidectomies, 3 other operations on the anal canal, 1 suture of a perforated duodenal ulcer in which the incision was contaminated at the time of operation, and 1 hemiglossectomy. There were thus 179 clean cases for analysis, and, as shown in Table I, 26 (14.5%) developed clinical signs of infection. From 8 (4.5%) of the wounds *Staph. aureus* was isolated.

TABLE I.—*Fate of 179 Clean Operation Wounds*

Clinical	Bacteriological	No. of Wounds
No sepsis	(Not all examined)	153
Sepsis	*Staph. aureus* isolated	8 (7)*
"	No *Staph. aureus*; Gram-negative bacilli isolated	7 (3)
"	No *Staph. aureus*; no specific organism recorded	8 (5)
"	Not examined	3 (1)
Total with sepsis		26 (16)

* Figures in parentheses indicate number of infections thought to have been acquired in the ward.

Sixteen of the 26 cases of sepsis and 7 of the 8 staphylococcal cases seemed to be due to ward infection. The decision to call a wound septic was a clinical one, and was founded on the presence of visible pus. Infection was considered to be probably acquired in the theatre rather than the ward when pus was found in the depths of the wound within a few days of operation, or when signs of infection were present at or before the first post-operative dressing.

Other Infections due to Staphylococci.—Six patients developed infections of the chest from which staphylococci were isolated; 4 developed staphylococcal infections of the skin, ear, or conjunctiva; one a staphylococcal urinary infection; and one a staphylococcal enterocolitis. Three patients were admitted with burns which became infected; one patient was admitted with a septic hand and another with a carbuncle, both due to staphylococci.

Staphylococci Responsible for Infection

Of the 311 patients admitted, 2 already had staphylococcal sepsis on admission and 17 (5.5%) developed staphylococcal wound sepsis or some other staphylococcal infection while in the ward. One of the patients with wound sepsis had been infected in the operating theatre. Of the remaining 16 patients, several had more than one focus of infection, so that there were 24 separate instances of staphylococcal disease acquired in the ward.

The phage types of the infecting staphylococci are shown in Table II. Of the 186 different phage types of staphylococci present at one time or another, only 13 caused disease, only 10 gave rise to ward infections, and only 3 were responsible for disease in more than one patient. These three types were all of phage-group III, and all were resistant to penicillin, streptomycin, and tetracycline.

The two patients admitted with septic lesions and the one infected in the theatre were infected with different types from those infected in the ward, and in no case did their type spread to other patients.

First Stages in the Return of Staphylococci to the Ward

Before giving an account of the sources of the infections just detailed it may be of interest to recount how the ward became recolonized with staphylococci at the beginning of our study.

When the ward reopened on the morning of September 25, 1956, members of the staff provided the only recognized

TABLE II.—*Phage-types of Staphylococci Causing Clinical Infections*

Phage Type	Antibiotic Sensitivity*			No. of Septic Lesions		Total No. of Patients with Septic Lesions	No. of Persons (Patients and Staff) Becoming Nasal Carriers
	Penicillin	Tetracycline	Streptomycin	Post-operative Wound Infection Acquired in Ward	Other Infections		
47/53/75/77 ...	—	—	—	1 abd. wound of prostatectomy	(Septic blister on same patient) 1 burn 1 chest (and tracheotomy in same patient)	3	6
6/42E/47/75w ...	—	—	—	0	1 conjunctivitis (1 otitis), 1 burn, 1 varicose ulcer	3	9
75/77	—	—	—	2 abd.-perineal exc. rectum† 1 gastrectomy	(Chest in all 3; enterocolitis in 1)	3	4
75/77	—	+	+	(1 abd.-perineal exc. rectum†)	1 burn	1	12
3C/55/71 + ...	+	+	..	1 orchidopexy		1	2
3C/55/71 ...	+	+	..	0	1 chest	1	1
7/47/53/54/75/77 ...	—	—	—	1 abd.-perineal exc. rectum	(Urinary tract, same patien)	1	3
6/47/53/75	—	—	—	1 ileal bladder, several wounds	0	1	2
29/80/42E ...	—	+	..	0	1 chest	1	2
80/6/7/47/53/54 ...	—	+	..	0	1 otitis	1	2

* + = Sensitive. — = Resistant to the antibiotic. ... = Not tested.
† 1 patient had an abdomino-perineal excision of rectum infected first with the 75/77-resistant and later with the 75/77-sensitive.
Note.—One thyroidectomy wound was infected in the operating theatre with a type 80 strain. One patient was admitted with a tenosynovitis due to type 55, and one with a carbuncle due to type 3B/55/71. All three strains were penicillin-sensitive. Lesions indicated within parentheses were in patients appearing elsewhere in the table with other lesions.

source of staphylococci. Twenty-one were examined, and 10 were found to be nasal carriers; of these not more than two carried the same type. In the afternoon they were joined by three patients, one of whom was a nasal carrier. During the day 185 cu. ft. (5.24 cubic metres) of air was examined but *Staph. aureus* was not found, and none was isolated from blankets on three empty beds or from two bed-curtains.

On the second day two more patients, both nasal carriers of *Staph. aureus*, were admitted. No staphylococci were isolated from bedding, curtains, bath, or wash-basin, but a lavatory seat yielded a staphylococcus of the type carried by one of the patients.

On the third day two more patients arrived, both staphylococcal carriers. Of 21 sweep plates and swabs from bedding, curtains, and toilet fittings, three yielded *Staph. aureus*. One of the positive cultures was from a drawsheet, and was the same type as that carried by the occupant of the bed; one was from a curtain with the type carried by the person taking the sweep, and the third was from a lavatory seat, this time with a different patient's staphylococcus.

By the end of the first week there were 12 patients in the ward, six being nasal carriers of different types of staphylococci. Re-examination of the staff showed that seven of the 21 were carriers of six different types. The air yielded 14 colonies of staphylococci of nine different types, of which seven were carried by patients and two were carried by the staff.

By the end of the second week there were 21 patients, 11 being carriers of 10 different types, and of the 23 members of the staff 13 were carriers, with not more than two carrying any one type. The air sample yielded 14 staphylococcal colonies, 11 of which were types carried by patients and one a type carried by a nurse; the source of two could not be traced.

Reservoirs of Infection

The sources from which patients could be infected included infected lesions, both septic and silently infected, carrier sites, inanimate objects, and air. We attempted to assess the load of infection under each of these headings, and in this section we describe the results obtained in the whole eight-months survey.

Infected Lesions.—The incidence of sepsis has already been discussed, and from this it is clear that at any one time there might be between 0 and 6 patients in the ward with some staphylococcal sepsis. We cannot indicate the incidence of prevalence of simple colonization of wounds, because, in the ordinary way, swabs were taken only when wounds appeared unhealthy.

Nasal Carriers.—The results of the examinations for nasal carriage conformed with what has been found elsewhere. Some 39% of patients swabbed during their first week in hospital carried *Staph. aureus* in the nose; the proportion tended to rise with increasing stay, so that about 60% of those swabbed in the third or later week were positive. Altogether 839 nasal swabs were examined from 96 members of the nursing, medical, and lay staff who worked in the ward at one time or another; 523 (62%) yielded *Staph. aureus*. Most of the carriers retained one type of staphylococcus at successive examinations, but, of the 96, 12 had two different phage types in successive cultures, three had three types, and one had four types.

Inanimate Sources

Staph. aureus was isolated from 284 of the 877 articles examined. In general the results reflected the carriage state of the person in contact with the article, or the general predominance of one type of staphylococcus in the ward at the time.

Staphylococci were isolated on 72 occasions from articles of bedding. These staphylococci were thought to be of the same phage type as those of the occupant of the bed on 27 occasions, of another patient in the ward at that time 31 times, and of a member of the staff 9 times; in 5 cases the source was not traced. Of the 18 drawsheets examined 12 yielded *Staph. aureus*: 9 strains were of the same type as that of the occupant of the bed and the other 3 were all of a type that was very widely spread in the ward at the time, apparently by a carrier with an ileostomy. Of the six negative drawsheets, five were from beds whose occupants were not nasal or faecal carriers of staphylococci.

Of 219 examinations of bed curtains 63 were positive for *Staph. aureus*: 19 of the strains were of the same type as that of an adjacent patient, 28 the same as that of another patient in the ward at the time, 12 were types carried by the staff, and 4 were not traced. Of samples of dust examined, 15 contained types traceable to patients, and one a type traceable to the staff. The speed with which contamination occurred was illustrated by one patient, a nasal and faecal carrier of staphylococci, who had contaminated his pillow, drawsheet, and bed-curtain within 24 hours of his admission to the ward.

Thus, in the circumstances of the ward that we studied, environmental contamination is more often attributable to patients than to staff. As time went by it became clear that under some circumstances some patients could shed staphylococci in great numbers. The presence of such patients was reflected in the results of air sampling.

Isolation of Staphylococci from the Air

After the first month of the study the air samples revealed the presence of an average of about 0.25 staphylococcus-carrying particle per cu. ft. (8.8 per cubic metre) of air.

But examination of the Chart shows immediately that such an average has little meaning: one of the most striking observations of the whole study has been the occurrence of successive waves of staphylococcal broadcast. Six major peaks in the air count were observed, and when the types of the air staphylococci were taken into account nine broadcasts could be recognized. During the first three and a half months, while routine sampling of articles was carried out, it was clear that they too showed this changing prevalence of different types, and it was in fact the close correlation of the types of staphylococci in the air with the types of those on articles that led us to give up routine sampling of the latter.

The fact that the staphylococcal broadcasts shown in the figure do not coincide with high general bacterial counts indicates that they were not due simply to occasional sampling at the time of some special disturbance—for example, bedmaking.

Spread of Staphylococci

A study was made of the genesis of the staphylococcal broadcasts just mentioned. Three typical examples are first described in some detail.

Spread of Type 6/42E/47/75w

This type (No. 8 in Chart) first appeared on January 18, 1957, in a patient's nose on the day after his admission, and it was subsequently isolated from his stool; he probably acquired it when a patient in another ward. As the strain was resistant to tetracycline the patient was isolated in a side-room on January 21, remaining there until March 15. The bedding and articles in the side-room became heavily contaminated, and the patient himself developed conjunctivitis and otitis media. He was undergoing deep x-ray therapy and had no wound to infect.

A staphylococcus of this type next appeared on February 25 in the nose of a patient in an adjoining side-room. This patient was ambulant, and as he distributed newspapers he moved freely through the ward, though not, officially, into the isolated side-room in which the first patient to carry the strain was nursed.

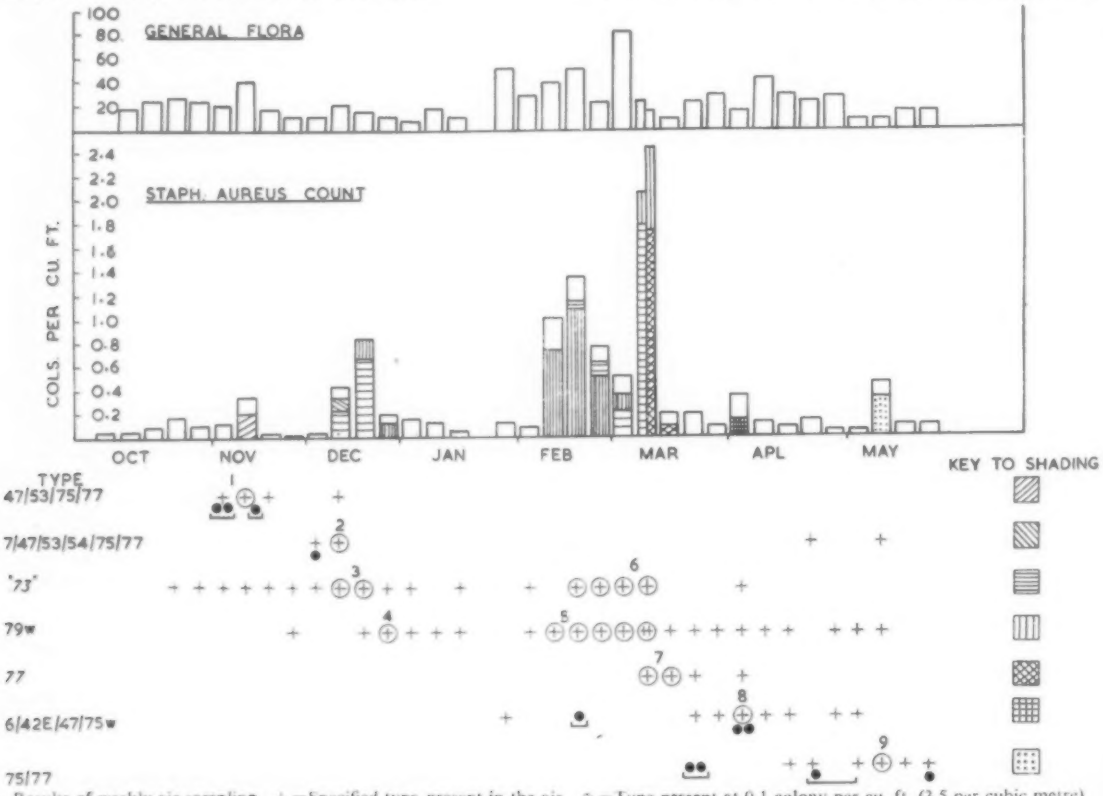
On April 3 a strain of type 6/42E/47/75w was isolated from a varicose ulcer of a patient who had been in the ward since February 4; how long before April it was present is unknown, as the ulcer had escaped swabbing. It was subsequently found at weekly intervals until the patient's discharge on May 16.

Also on April 3, staphylococci of the same type were isolated from a burn of a patient who had had the strain for the first time in his nose on April 1. This patient left on April 7. On the next day (April 8) type 6/42E/47/75w was isolated from the noses of four other patients; it was carried in the nose by one more patient in the next week. During the course of the following week three of these patients were discharged, and one was isolated in a side-room and his nose treated with neomycin cream. The type was not isolated again from patients apart from the varicose ulcer.

From the air the strain was isolated in small numbers in samples taken on March 19 and 26. On April 2, at about the time when the strain infected the burn, the air contamination increased to about 0.17 colony per cu. ft. (6 per cubic metre) of air. The count was 0.03 and 0.02 colony per cu. ft. (1.05 and 0.7 per cubic metre) respectively on April 8 and May 3, and none was found thereafter.

Type 47/53/75/77

We could not trace the way in which this strain (No. 1 in Chart) entered the ward. It was first isolated on



Results of weekly air sampling. + = Specified type present in the air. ⊕ = Type present at 0.1 colony per cu. ft. (3.5 per cubic metre) or more; the actual count is indicated by the hatching in the column above. ● = Cases of infection occurring in the ward. Numerals refer to the incidents of broadcasting detailed in Table III. Sampling was ordinarily carried out on one day in each week, but samples were taken on two days in the week of March 7, and as the type distribution differed considerably the results of both are entered.

October 22 from a bed-curtain and subsequently on October 31 from a towel in the sterilizing room, and on November 2 from two bedspreads. One of the two beds was empty and the other was occupied by a patient who was not carrying or infected with staphylococci.

The strain was first isolated from a person on November 5 when it was recovered from an anal wound of a patient admitted unconscious on November 2. On November 5 it was also isolated from a nasal swab of a patient admitted on November 3 and from another patient with extensive burns. This last patient had been in the ward between November 1 and 2, but thereafter remained isolated in a side-room until his discharge on November 12. On November 8 type 47/53/75/77 was found to be infecting the tracheotomy wound and sputum of the patient admitted unconscious on November 2, who was then moved to isolation in the second side-room, where he stayed until he died on November 10.

At this stage there were indications that further spread of the strain was beginning, and by November 12 three more patients, all of whom had had a different type before, carried type 47/53/75/77 in their noses. It had infected one more patient's wound, and by the time this patient was isolated on November 16 it had produced a septic blister on him. The patient was discharged on December 3, and, after the remaining two carriers in the ward had lost the type from their noses, it disappeared.

The various incidents were reflected in air counts. No colonies were found on October 29; on November 5 the count was 0.03 colony per cu. ft. (1.05 per cubic metre), on November 12 it was 0.20 (7.6), on November 20 less than 0.01 (0.35), and none was found on November 27.

Type 79w

This penicillin-resistant tetracycline-sensitive staphylococcus (Nos. 4 and 5 in Chart) colonized the noses of 15 members of the staff and 42 patients, and was found on articles and in the air, but was not responsible for any sepsis. It was apparently brought into the ward by a nurse, who, although a heavy carrier, did not appear to shed the strain freely. She was in the ward from September 24 until December 4, but in that period her staphylococci were not isolated from any article, and only two colonies were isolated from air. On November 19 the nurse was joined by another carrier of the same type, but this girl too was presumably not a heavy shedder.

The most likely source for the brisk spread of the type, which began in the second half of December, was a patient admitted on November 24 who had acquired the strain in his nose by December 3. This patient had a septic wound, but swabs on December 10 and January 2 failed to show staphylococci. Because of the infection the wound was dressed at intervals of two to four hours from December 8 to 11, and until January 4 twice daily. Staphylococci of type 79w were present on the patient's bedding, and the upheaval which the frequent dressings necessitated presumably threw them into the air. By the end of December this type had colonized four nurses' and nine patients' noses, and had been isolated on 21 occasions from bedding and curtains at both sides and both ends of the ward. Two colonies (less than 0.01 per cu. ft.—less than 0.35 per cubic metre) were isolated on November 27. Thereafter the air counts were 0.12 colony per cu. ft. (4.24 per cubic metre) on December 18 and 0.11 per cu. ft. (3.88 per cubic metre) on December 24.

By the time the patient was discharged on January 2 this staphylococcus was plainly well entrenched, and it stayed as a common type in the ward for the next three months. In this time it colonized the noses of 11 more members of the staff and 20 patients, and it was isolated from three wounds, none of which, however, was regarded clinically as being infected.

Between January 1 and April 8, 2,290 cu. ft. (64.5 cubic metres) of air were examined. From this amount 1,006 colonies of staphylococci were isolated and 390 were typed: 147 belonged to 79w. There was one peak period from February 11 to February 21 when 391 colonies of staphylococci were isolated from 410 cu. ft. (11.6 cubic metres) of air. Of these colonies 108 were typed, 81 belonging to type 79w. The reason for this rise was not found.

At the beginning of April five patients carried this type in their noses: by the middle of the month they had been discharged, and until the end of the investigation the only carriers left were four nurses. With patients eliminated there was very little aerial shedding, and after April 8 only an occasional colony was isolated from the air (5 colonies from 1,531 cu. ft.—43.4 cubic metres).

Summary of Staphylococcal Broadcasts

In Table III we have summarized the information about the nine staphylococcal broadcasts that can be distinguished

TABLE III.—*Details of Nine Incidents of Staphylococcal Broadcast*

Key to Chart	Type	Date of 1st Isolation	Date of Last Isolation	Source from which First Isolated	Source from which Probably Dispersed	Wounds at Risk During Period of Dispersal: Total Wounds at Risk	Wounds at Risk During Period of Dispersal: Average No. of Dressings per Day	No. Patients Developing Septic Lesions	No. Becoming Nasal Carriers: Patients	No. Becoming Nasal Carriers: Staff
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
1	47/53/75/77	Oct. 22	Dec. 11	Bed curtain	Sputum of unconscious pt.	15	8	3	6	0
2	7/47/53/54/75/77	Nov. 19	,, 21	Nose of pt.; already in ward air	Urinary infection	18	8	1	3	0
3	"*73*"*	Oct. 3	See 6	Nose of pt.	Ileostomy (though evidence for infection not good)	24	8	0 (doubtful infection of ileostomy)	3	0
4	79w	Sept. 24	,, 5	Nose of nurse	Nose of pt.; frequent bedmaking; wound not adequately swabbed	13	6	0†	15	7
5	79w	See 4	May 31	See 4	Not known. (? Unrecognized infection of wound)	30	7	0	27 new	8 new
6	"*73*"	,, 3	Apr. 2	,, 3	Not known	27	7	0	4	0
7	77	Mar. 7	,, 2	Air	Not known; never found on patient or staff	18	7	0	0	0
8	6/42E/47/75w	Jan. 18	May 13	Nose of pt.; ? acquired in another ward	Burns of different pt.	20	8	3	9	0
9‡	75/77 tet. sens.	Apr. 23	Later than May 31	Nose of pt.; ? acquired in ward or earlier	Frequent dressings and bedmaking of same pt.	23	7	1	13	1
	75/77 tet. res.	? Mar. 11	May 13	Patient from another ward	—			3	3	0

* Type "*73*" included a number of strains with rather variable patterns of phage reactions, lysis by phase 73 used at a strong concentration being the most characteristic reaction.

† At least three wounds became colonized but not septic.

‡ The drug sensitivity of the strains from the air was not determined.

in the air sampling records given in the Chart. Four of the seven different staphylococcal types were apparently introduced by nasal carriers, in two cases probably infected in other wards of the hospital. The origin of the other types is not known, though the first two in Table III (47/53/75/77 and 7/47/53/54/75/77) were probably derived from elsewhere in the hospital.

It is more difficult to specify the source of the broadcasting into the air of the ward, and several of the entries in column 6 of Table III are open to some doubt. With the exception of type 77 there were always nasal carriers of the strain in the ward at the material time, but we cannot tell whether they, or some patient with an unrecognized subclinical infection of a wound, was responsible for spread in the incidents given as "not known" in column 6. It was of interest, however, that there was only one instance in which the staphylococci were probably dispersed by the person who introduced the strain into the ward.

When the phage types listed in Table III are compared with those that were observed causing sepsis (Table II) it is immediately clear that a wide dispersal of a single type might be quite unrelated to sepsis. In comparing the different types, however, it needs to be remembered that the patients infected with tetracycline-resistant strains (incidents 1, 2, 8, and 9) were nursed in isolation. Had they been nursed in the open ward the degree of dispersal might have been as great as in incidents 5, 6, and 7.

There was also a wide variation in the extent to which different staphylococci colonized noses: type 79w colonized many noses of patients and staff, while type "*73*" colonized only seven noses, and this despite the fact that both types were present in the air in large numbers and over a considerable period.

An additional indication that some people shed staphylococci more freely than others was provided by a comparison of the types carried by people with the types found on articles or in the air. From people 152 different types were isolated, but only 44 types were isolated from articles. Again, the 946 air staphylococci typed belonged to 71 different phage types, but only 25 of these types occurred three or more times.

Discussion

In the summer of 1956, at a time when numerous cases of staphylococcal sepsis were occurring in the ward, *Staph. aureus* of the epidemic type was found widely spread in the air and on bedclothes, bed-curtains, and the like (Shooter *et al.*, 1957). This observation raised several questions. Did the heavy air contamination represent spread from one or more especially active dispersers, or did it merely reflect the number of infected patients in the ward? Was the staphylococcus actually spread to new hosts by way of the air, or was the aerial contamination merely a by-product of spread by other routes? Could the counts of *Staph. aureus* in the ward air be used to measure the risk that infection might spread among the patients? Did the spread of one particular type of staphylococcus reflect the chance presence of a dangerous disperser of that type, or was the staphylococcus a specially virulent one?

Eight months' further study of the ward that suffered the 1956 epidemic could not be expected to answer these queries completely, but it has served to clarify some of the issues.

To us the most striking feature of our survey has been the occurrence of successive waves of staphylococcal broadcast due to different staphylococci and each apparently due to a different patient. A succession of different types infecting the patients in a ward has been noted in maternity units—for example, Hutchison and Bowman (1957) and Baldwin, Rheins, Sylvester, and Shaffer (1957)—but in our study it was the succession of environmental broadcasts that was so striking. There was no obvious relation between the degree of environmental contamination in these broadcasts and the development of sepsis in the susceptible wounds in the ward except that no staphylococcus spread to wounds without some evidence of broadcast to air and articles. It was clear that extensive contamination of the air and environment could result from dispersal from a single person. We still do not know whether, when staphylococci spread to other wounds, they spread through the air, though it is reasonable to think that this was the course by which the noses of staff and patients were colonized.

That some people shed staphylococci more readily than others also seemed clear. On some occasions this shedding could be related to the sort of wound that they had, or the frequency with which it was dressed. While the lack of correlation between the level of aerial contamination and the incidence of sepsis indicates that air sampling cannot be used alone to predict outbreaks of wound infection, it can be used to detect persons who are likely to disperse bacteria. By more extensive studies it ought to be possible to define circumstances in which potential dispersal should be assumed without need for individual testing, and such studies would also show how common are the healthy heavy dispersers described by Hare and Thomas (1956).

Although the failure of some of the types of *Staph. aureus* to cause secondary cases of sepsis may have been due to a lack of truly susceptible wounds in the ward at the time, this seems unlikely, and it is more reasonable to think that the strains that spread were the more virulent strains. Until recently there was no good evidence that virulence varied greatly among coagulase-positive staphylococci. During the last few years, however, epidemics of infection in maternity units due to staphylococci of phage-type 80 (and the same or closely related strains reported in American literature as 52/42B/42C/44A/80/81, etc.) have demonstrated unequivocally that such variations exist.

As a tentative hypothesis we may distinguish three different ways in which surgical patients may be infected by staphylococci, apart, that is, from the case where a particular dangerous carrier is concerned (see McDonald and Timbury, 1957).

At the time of operation patients may be susceptible to infection by staphylococci of many different phage types, as seemed to be the case in the unit reported by Shooter *et al.* (1956); this susceptibility might be due to a depression of resistance, or simply to the fact that the organisms can be deposited deeply in the tissues.

In the ward, patients are clearly exposed to a great number of different staphylococci—both those that they carry themselves and those carried by other people. Most of these staphylococci are probably of relatively low virulence, and perhaps patients become infected with them only when subjected to a large dose, so that in the ordinary way the incidence of infection is an index of the standard of asepsis attained.

From time to time a ward may be invaded by staphylococci that are more virulent, such as some strains of type 80, or the types like 75/77, 47/53/75/77, and 6/42E/47/75w that we encountered. It is unlikely that these strains are spread any more easily than less virulent staphylococci, but there seems little doubt that they cause infection more easily and that conventional nursing techniques will not entirely control them.

Of the 24 infections that we observed 16 were due to three types of staphylococci, and the remaining eight were due to seven different types. The low incidence of these "sporadic" infections may well be attributable to the adequacy of the equipment and staffing of the ward.

We believe that, in our ward, barrier nursing in a side-room of patients with the more virulent strains was an effective method of isolation. Furthermore, we believe that, by isolating patients infected with these few strains, we prevented widespread infection. Again, the effectiveness of this measure may have been due to the favourable circumstances. Under less propitious conditions both the sporadic infections might be more common, so that some of the

staphylococci that appeared avirulent to us could infect wounds, and also the simple form of isolation might not suffice to prevent the spread of the virulent strains. Only trial will tell.

Summary

During an eight-months survey, 311 patients were admitted to a general surgical ward and 17 (5.5%) developed staphylococcal wound sepsis or some other staphylococcal infection (for example, pneumonia, urinary infection, entero-colitis) while in the ward. Only one of the eight cases of wound sepsis was attributable to infection in the operating theatre.

The reservoirs of staphylococci in nasal carriers and in inanimate objects and the air were examined regularly, and staphylococci from all these sources, as well as from patients' wounds, were examined for bacteriophage type.

Some 186 different types of *Staph. aureus* were recognized, but only 13 of these caused disease, and only three were responsible for disease in more than one patient.

The air and dust sampling revealed nine occasions when staphylococci of a single phage type reached the level of 0.1 particle per cu. ft. (3.5 per cubic metre) of air. These nine broadcasts were due to seven different types of staphylococci; the three types that were present in the air in the greatest numbers failed to cause any manifest secondary infections. This, and the fact that there were so many types of staphylococci that never caused sepsis, suggested that some staphylococci were more "virulent" than others.

Several of the staphylococcal broadcasts could be attributed to patients with infected lesions who were peculiarly apt to disperse, such as an infected tracheotomy wound, infected urine in an incontinent patient, an infected wound requiring very frequent redressing.

Patients infected with tetracycline-resistant staphylococci were, when possible, barrier-nursed in a side-room. This appeared to be effective in limiting the spread of their infection. Ten patients (with four different types) were nursed in isolation, and only one secondary case appeared in the ward.

We are indebted to Mr. C. Naunton Morgan and Mr. D. F. Ellison Nash for permission to make these observations in their ward. Our thanks are also due to the Medical Research Council for a grant in support of the work, and to Miss P. M. Davies and Miss Anne Deacon for laboratory assistance.

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The Nuffield Provincial Hospitals Trust has approved a grant of £7,500 spread over three years to assist in the establishment of a sheltered workshop, for long-stay patients with chronic psychotic illnesses, at Cheadle Royal Hospital, Cheshire. The project will be under the direction of the senior medical hospital staff. The Trust is also providing £1,500 for an investigation into the cost of mental illness.

LONG-TERM RESULTS OF VAGOTOMY AND GASTRO-ENTEROSTOMY IN CHRONIC DUODENAL ULCERATION

A COMPARISON WITH GASTRECTOMY

BY

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AND

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In 1950 one of us (H. B.) initiated an investigation into the results of vagal-nerve section in the treatment of chronic duodenal ulceration. Mr. A. V. Pollock was invited to undertake this work. Some 1,300 cases were collected from teaching and non-teaching hospitals in this country. This series included 489 cases treated by vagotomy and gastro-enterostomy (Pollock, 1952). It was decided to file the names and addresses of these patients and to use them as the basis of a long-term study. In 1955 Mr. John Lloyd Davies undertook a review of these cases, and his results were published (Lloyd Davies, 1956). Of the initial cases, permission to study was granted in 198, and these formed the basis of his report. We have now, two years later, made a further study of these cases, and we have been able to add a further 103 of the original series. We now therefore report on 301 cases, the earliest being seven years after operation and the latest nine.

This review has been made by questionary and personal interview. The series included 69 war pensioners, but, while they have been included for the purpose of assessing the proved recurrence rate, they have been omitted in our studies of post-operative symptomatology. In another group of 103 cases the follow-up study was made on our behalf by the department of surgery concerned. In assessing the post-operative picture with regard to symptoms, we have chosen to limit ourselves to a series of 130 cases which we have ourselves investigated.

Of this series of 301 cases, only six are untraced and 13 have died from causes known to have no connexion with peptic ulceration, leaving 282 cases followed to seven to nine years after operation.

Analysis of the Post-operative State

Mortality.—One of us (H. B.) used this operation in 1949 and 1950 but stopped using it then because its results were unknown. We did, however, come to use it again when the results of Mr. Lloyd Davies's work became known, and we have used it in all cases of duodenal ulceration needing surgical treatment since that time. We can report a series of approximately 100 cases without a death. Other workers have reported a very low mortality from this operation. Crile (1952) recorded 0.4% mortality in 445 patients and Hoerr (1953) a mortality of 0.5%.

Recurrence Rate.—The proved recurrence rate, as shown by perforation, haemorrhage, or operation, has been found to be 4.25%. As is discussed below, this figure must be considered in the light of evidence of a high incidence of incomplete nerve section.

Nutritional State.—One feature of this operation is that the patients are able to eat meals of normal size. It is not

surprising, therefore, to find that the nutritional state is good. Weight has been gained in 14%, has remained steady in 75%, and has been lost in 11%.

Post-operative Anaemia.—Post-operative haemoglobin investigations were done on an unselected group of 50 cases from this series. Eight years after operation only one of the 50 had a haemoglobin level below 85%. This reading was 84%, and the same case was one of suspected tuberculosis. Of the remaining 49 patients, 12% were found to have a haemoglobin level below 90%. These figures show that anaemia, at eight years, is not a common complication of this operation.

Physical State.—Approximately one-third of this series were interviewed personally and inquiry made into their work and physical state. It was found that many were occupied in heavy work, and in no case was the ability to undertake it reduced.

Change of Bowel Habit.—To the question, " Do you have diarrhoea or loose motions ? " 30% of patients replied in the affirmative. In our series the incidence of this symptom is approximately the same in all surgical centres from which these cases were drawn. We inquired further into the bowel habit of these 30% and we found that the symptoms take on a specific pattern consisting of bouts of diarrhoea or loose motions lasting from one to three days, with three or four loose or liquid motions daily. These attacks recur at intervals varying from one to three months, and between attacks the patient is symptom-free. Many other patients state that the bowel habit has been improved by the operation in that they no longer have constipation and that their motions are now regular and not hard. This symptom of diarrhoea or loose motions appears to cause little disability ; only direct questioning has brought it to light. We have found no patient who has sought advice for it. The mechanism of this symptom is not clear. *X*-ray examination has failed to show gastric delay or intestinal hurry. We are at present engaged in further investigation into this problem.

Post-cibal Symptoms.—It has long been known that post-cibal symptoms occur after gastro-enterostomy, though much less frequently and with less severity than after partial gastrectomy. The incidence in this series is 16%. Symptoms were mild and no case of severe " dumping " was recorded.

Bilious Regurgitation.—This was found in 13% of cases and was regarded as secondary to the gastro-enterostomy.

Comparison with Gastrectomy

Mortality.—The mortality of gastrectomy in expert hands is probably 1–2%, but it seems that the overall mortality in this country is a good deal higher. The operation of vagotomy and gastro-enterostomy exposes the patient to almost no risk either of mortality or of post-operative morbidity, for there is no inherent risk in the operation as there is in partial gastrectomy. We may regard the risk as that of gastrectomy less its inherent risks of stump leakage, haemorrhage, and loop obstruction.

Recurrence Rate.—The proved recurrence rate of ulceration after partial gastrectomy probably varies from 2% to 6%, depending upon the extent of gastric resection. The proved recurrence rate in our series of vagotomy and gastro-enterostomy is 4.25% at eight years. Again we emphasize the high incidence of incomplete nerve section in this series.

Nutritional State.—It is well known that after gastrectomy many patients cannot eat full meals, and, perhaps as a result of this, loss of weight is not uncommon. Ivy, Grossman, and Bachrach (1950) found the post-operative weight steady or increased in 53% and decreased in 47%. This is a very different figure from our findings after vagotomy and gastro-enterostomy, in which only 10% showed weight loss.

Post-operative Anaemia.—One of us (H. B.) has investigated anaemia after partial gastrectomy. The incidence of microcytic anaemia was shown to increase considerably with the passing years. A study of 300 male patients, 50 in each year group from one to six years after Polya gastrectomy, is shown in the Table. It will be seen that post-operative anaemia after gastrectomy is a common condition. Often undiagnosed and untreated, it can result in considerable disability. As stated above, at eight years anaemia does not appear to be a complication of vagotomy and gastro-enterostomy.

Post-operative Incidence of Anaemia

Haemoglobin	Years after Gastrectomy					
	1	2	3	4	5	6
	%	%	%	%	%	%
Under 85% ..	12	12	22	32	38	58
,, 80% ..	6	8	10	20	26	36
,, 75% ..	2	6	4	14	18	24
,, 70% ..	0	0	0	4	6	18

Physical State.—The physical fitness of patients after vagotomy and gastro-enterostomy is very much better than after gastrectomy. Not many patients return to heavy manual work after gastrectomy.

Change of Bowel Habit.—We have written already at some length about this symptom after vagotomy and short circuit. The same symptom occurs after gastrectomy and, as with vagotomy and short circuit, it has been brought to light only by direct questioning. In a series of 200 post-gastrectomy patients, in reply to the direct question, " Do you have diarrhoea or loose motions ? " 20% replied in the affirmative. This compares with 30% after vagotomy and short circuit. Exactly the same pattern exists in both operations, but the attacks occur somewhat less often after gastrectomy.

Post-cibal Symptoms.—There is no need to state here the incidence and severity of post-cibal symptoms after gastrectomy. These are only too well known. It is generally agreed that the incidence and severity of these symptoms after gastrectomy are related to the extent of gastric resection. The operation of vagotomy and short circuit carries with it a much lower incidence and less disability.

Bilious Regurgitation.—As with the post-cibal " dumping " symptoms, so with bilious regurgitation, the incidence and severity are much less after vagotomy and gastro-enterostomy than after gastrectomy.

Discussion

We believe that all workers who have studied these two operations will agree that, given no increased incidence of recurrent ulceration, vagotomy and gastro-enterostomy is a better operation than gastrectomy. The proved recurrence rate in this series is within the limits sometimes given for gastrectomy. Unfortunately we have no record of the number of nerve trunks found in this series of cases, but we think that the finding of three or four nerve trunks was not common at that time. Anatomical studies of the number of vagus-nerve trunks in man at this level have been made by several workers (Chamberlin and Winship, 1947 ; Dragstedt *et al.*, 1947 ; Jackson, 1949). It seems that only two nerve trunks were found to be present in approximately 80% of cadavers. It is, however, interesting that, since we have used, during operation, a test for completeness of nerve-trunk section, we have found in our small series of 16 patients only 2 (12.5%) with two nerve trunks. The remaining 14 (88%) have had three or more trunks.

There is good evidence that, at the time these cases were operated on, there was a high incidence of incomplete nerve section. We know of two cases in which the surgeon failed to find the anterior nerve. Both these cases developed anastomotic ulceration shortly afterwards. It is clear from many studies that incomplete nerve section, as shown by the insulin test meal, was common at this time. Lloyd Davies (1956) found that a positive insulin test was present in every case of recurrent ulceration where the results of this investigation were known.

Now that a method of proving completeness of nerve-trunk section can be used during operation (Burge and Vane, 1958), it may be that the recurrence rate after this operation will be

reduced to a figure as low as, or lower than, the best after gastrectomy.

We at one time thought that the incidence of changed bowel habit after vagal-nerve section might weigh in favour of gastrectomy. However, a study of these symptoms after gastrectomy reveals exactly the same problem, although to a somewhat less degree.

In trying to assess the place of vagotomy and gastro-enterostomy, we do not believe that it is indicated only in certain types of patient, as, for example, in women and elderly men. If it is to be used at all, then in our view it should be used in all cases where surgery is necessary. In the present state of our knowledge, based on this eight-year study, we believe that, given complete nerve-trunk section, vagotomy and gastro-enterostomy is the operation of choice. At one time we thought that a surgeon experienced in this operation could in every case achieve complete nerve-trunk section without the use of a test. Since such a test has been available we have satisfied ourselves that this is not true and that even an experienced surgeon will obtain better results with this help.

It will be interesting, in the future, to study the late results of this operation in cases in which complete nerve-trunk section has been proved at operation.

Summary

301 cases, of which only 6 are untraced, of duodenal ulceration treated by vagotomy and gastro-enterostomy are reported. All patients have been followed up for at least seven years. The proved recurrence rate was 4.25%, and this in spite of evidence of a high rate of incomplete nerve section. There has been no proved recurrence in this series since an earlier review in 1955.

The results of this operation are compared with those of gastrectomy, and it is concluded that vagotomy and gastro-enterostomy is a better operation so long as there is no great increase in the recurrence rate as shown by a long-term study. From the point of view of nutritional state, anaemia, maintenance of weight and ability for heavy work, vagotomy and gastro-enterostomy is more satisfactory than gastrectomy. The only less favourable symptom after this operation is some looseness of the bowels, which takes on the picture of occasional loose motions. This same symptom, with the same pattern though in somewhat milder form, is found to occur also after gastrectomy. No patient in this series seems to have sought advice for this symptom.

This high incidence of incomplete nerve section in the past is good evidence that this operation is better undertaken with the help of a test for complete nerve trunk section which can be used *during* operation. Such a test is now available (Burge and Vane, 1958).

It is concluded that vagotomy and gastro-enterostomy is the operation of choice in either sex and at any age when surgery is indicated for chronic duodenal ulceration.

This investigation has been made possible by the financial help of the Dan Mason Research Foundation of the West London Hospital Medical School. We thank all those surgeons who so kindly gave permission for us to follow their cases through all these years. We would thank the Ministry of Pensions and National Insurance for permission to study the war pensions cases. We are especially indebted to Mr. I. F. McNeill for the time and work he so kindly gave to these investigations.

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METHOD OF TESTING FOR COMPLETE NERVE SECTION DURING VAGOTOMY

BY

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The method described here was devised to allow the surgeon to test the completeness of vagotomy before the abdomen was closed. It consists in the application of a simple physiological technique to the human and, as such, was first validated on cats. It has now been applied successfully to patients, and is both safe and reliable.

Method

Cats.—Cats were anaesthetized with chloralose (80 mg./kg.). The blood pressure was recorded on a kymograph with a mercury manometer connected to a cannula in the left carotid artery. The intragastric pressure was also recorded on the kymograph, using a water manometer connected through the system, as shown in Fig. 1, to a tube

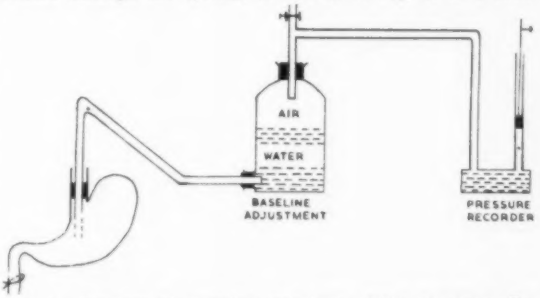

FIG. 1.—Diagram of recording technique. With the screw clip on the top inlet of the bottle open, the stomach can be filled with a known amount of water. The clip is then closed and the bottle moved up or down to bring the baseline on the pressure recorder to a convenient level.

passed down the oesophagus into the stomach. The oesophagus was sealed by an inflated cuff on the gastric tube and the pylorus was occluded by ligation. The stomach was distended with warm water. Platinum electrodes were used to stimulate the vagus nerves, either in the neck or on the oesophagus above or below the diaphragm with the chest open. Square wave pulses (0.5–25/second frequency, 0–50 volts, and 0.5–5 milliseconds' duration) were applied through the electrodes for periods of from 0.5–2 minutes. In some animals electrodes were made to encircle the oesophagus to correspond with the technique to be applied in man.

Man.—The patient was anaesthetized with thiopentone and nitrous oxide. Gallamine triethiodide was used to achieve muscular relaxation. Because the method depends upon recording the effects of vagal-nerve stimulation upon stomach motility, premedication with atropine or atropine-like drugs was avoided. Atropine was given during the operation after the test was finished. The abdomen was opened by a left upper paramedian incision; the left coronary ligament of the liver was divided to allow the left hepatic lobe to be retracted to the right. A small rubber tube was placed around the lower oesophagus for traction. There has been no difficulty in ensuring that the posterior vagus nerves were included within this tube. The upper part of the small omentum was divided between ligatures to give a better exposure of the lower oesophagus. A large-bore cuffed rubber tube was passed by the mouth until its

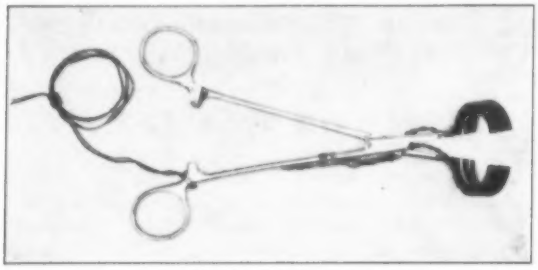

FIG. 2.—Electrodes.

tip was in the stomach. The electrodes designed for this operation (Fig. 2) were applied and the cuff on the tube was inflated. In this way the oesophagus was sealed and the vagus nerves were brought into contact with the electrodes. The pyloric antrum was occluded with a light intestinal clamp and the stomach filled with 0.5–1.5 litres of warm water, depending on its size. In early cases the recording apparatus was similar to that shown in Fig. 1, using a 2-litre aspirator for the baseline adjustment and filling-bottle. In the later cases an ink-writing bellows pressure recorder was used (Fig. 3).

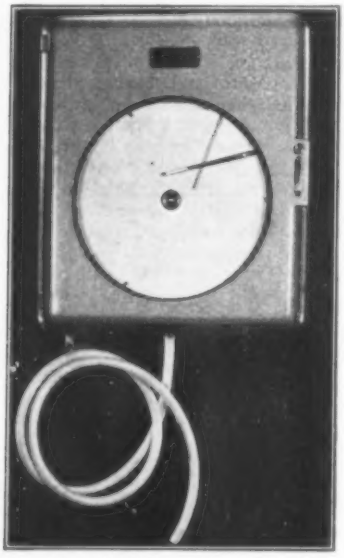

FIG. 3.—Ink-writing pressure recorder.

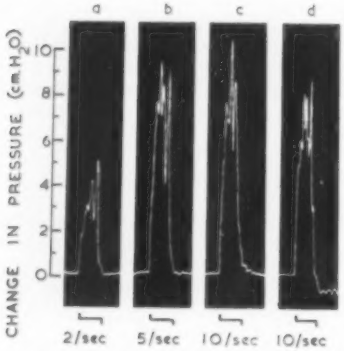

FIG. 4.—Kymograph tracing of gastric pressure responses to vagal-nerve stimulation in the cat. The stomach was distended with 50 ml. of saline. The vagus nerves were stimulated with platinum electrodes in the neck with 2 ms. shocks at 10 volts. (*a*) Both vagi stimulated at 2/sec for 1 minute. (*b*) Both vagi stimulated at 5/sec. for 1 minute. (*c*) Both vagi stimulated at 10/sec. for 1 minute. (*d*) Left vagus stimulated at 10/sec. for 1 minute.

Results in Cats

Stimulation of the vagus nerves is well known to cause a generalized contraction of the stomach, leading to a rise in intragastric pressure. The strength of the contraction depends on several factors, such as the frequency and voltage of stimulation and the initial distension of the stomach. Previous work (Paton and Vane, 1956) had defined some of the conditions necessary for obtaining maximal contractions of the isolated guinea-pig stomach in response to vagal stimulation; the response of the cat stomach *in situ* was found to vary in a similar way.

To obtain a maximal contraction in the cat it was found that stimuli of 2 ms. duration and up to 20 volts in strength were sufficient. The optimal frequency of stimulation was between 2 and 5/seconds in most animals (Fig. 4). Stimulation of one vagus nerve in the neck for one to two minutes produced an increase of pressure which was equal to, or nearly equal to, the maximal response elicited by stimulation of both vagus nerves.

The vagus system was dissected on the lower oesophagus with the chest opened and four to six nerve trunks were found. When all but one was divided and the vagus nerve stimulated in the neck, an increase in gastric pressure could still be recorded. In one cat, with the chest opened and the diaphragm divided, the circular electrodes were used to stimulate the vagus nerves just above the stomach. In this cat there were only two nerve trunks at this level. It was found that section of one of these two trunks failed to modify the response to stimulation. The remaining anterior trunk was then partially divided so that about one-half remained intact. On stimulation, a good response was obtained. What remained of the trunk was again halved, leaving now only a fraction of the whole nerve intact. In spite of this division, changes in gastric pressure were clearly recorded on stimulation. It this way we were able to conclude that the test was sensitive enough to record even small undivided nerve trunks.

Results in Man

It was not possible to study the parameters of stimulation in man to the same extent as in the cat, but in the first two cases various frequencies of stimulation were used. In each instance a frequency of 10/second gave a maximal contraction. Lower frequencies gave smaller contractions, whereas frequencies higher than 10/second had no greater effect. This frequency was therefore chosen for subsequent operations. The voltage of stimulation was also varied in the first two patients, and it was found that between 10 and 20 volts was sufficient to induce a maximal response in a one- to two-minute period of stimulation. It must be remembered, however, that the voltage needed depends not only upon the design of the electrode but also upon the amount of connective tissue covering the vagus nerves. It is therefore better to use a voltage of stimulation which is likely to be supramaximal, and in subsequent cases the voltage was set at between 40 and 50 volts.

The amount of fluid in the stomach is also important, for the magnitude of contraction depends upon the initial volume. In the first patient the vagus nerves were stimulated at the same frequency (10/second) with 0.5, 1, and 1.5 litres of water in the stomach. At 0.5 litre no contraction was obtained, but at both 1 and 1.5 litres the pressure increase was about 10 cm. of water. In subsequent patients the amount of filling was adjusted to give a basal pressure on the recorder of about 3 cm. of water. This was usually achieved with 0.5–1 litre in the stomach.

After recording the change in gastric pressure in response to stimulation with all nerves intact, the electrodes were removed and one nerve trunk was cut. About 2 in. (5 cm.) of the nerve was removed and a ligature tied to the peripheral end so that it could be kept away from the electrode. The test was repeated after section of each nerve trunk until stimulation no longer produced a contraction, indicating that all the nerves had been found and sectioned. The surgeon found it more convenient if the stomach was emptied after each stimulation. The operative area was also more available to the surgeon if the stomach tube was withdrawn from the lower oesophagus.

In one patient, after a control stimulation, all the nerves that could be found were cut. The electrodes were then replaced and the area was stimulated to ensure that no nerve remained in continuity. It is this procedure that is to be used routinely.

Fig. 5 shows a tracing obtained from one of the patients. Between each part of the tracing a nerve trunk (later proved

by histological examination) was removed. It can be seen that the contraction remained quite large until the third and fourth trunks were sectioned. In all patients frequent blood-pressure readings and E.C.G. records were taken.

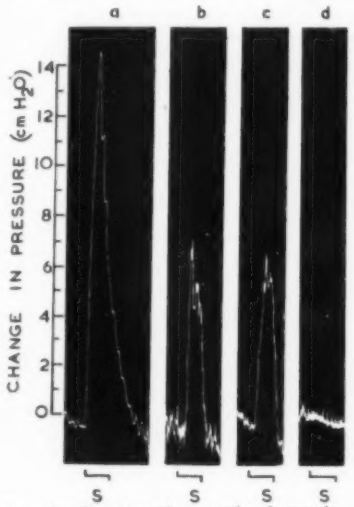

FIG. 5.—Kymograph record of gastric pressure responses to vagal-nerve stimulation in man. The stomach was distended with 0.7 litre of water. The vagus nerves were stimulated on the oesophagus below the diaphragm with 2 ms. shocks at 10/second and at 45 volts for 1½-minute periods. (*a*) Before nerve section. (*b*) After section of first major nerve trunk. (*c*) After section of second major nerve trunk. (*d*) After section of third and fourth major nerve trunks.

Stimulation of the vagus nerves had no effect on blood pressure, heart rate, or form of the E.C.G. In one patient stimulation of the vagus induced diaphragmatic movements, presumably by current spread. This movement was readily abolished by a further injection of gallamine triethiodide.

It is usual to record fluctuations in gastric pressure with each respiratory phase. To avoid these fluctuations, respiration was completely abolished during stimulation in the later cases.

After the test had demonstrated complete nerve-trunk section the operation was completed by making a posterior vertical isoperistaltic gastro-enterostomy. In the present work we have used this method of gastric drainage rather than pyloroplasty.

Recently an improved electrode has been developed which allows localization of the nerve trunks. Each semicircular band of silver was divided into two segments. In this way four pairs of electrodes were formed, and each was wired separately. Using a rotary switch, the stimulus was applied to the four quadrants in turn.

In this way the nerve trunks were localized to their quadrants before nerve section was attempted. Similarly, any small nerve trunk not found at the time of nerve section was not only demonstrated but also localized to its quadrant. The search for any such small nerve was made easier and more satisfactory in this way.

Number of Nerve Trunks Capable of Causing Gastric Contraction

Case No.	No. of Nerve Trunks		
	Anterior	Posterior	Total
1	1	2	3
2	2	1	3
3	3	2	5
4	2	2	4
5	1	2	3
6	1	1	2
7	1	2	3
8	1	2	3
9	1	1	2
10	2	3	5
11	4	3	7
12	1	2	3
13	2	2	4
14	2	1	3
15	2	2	4
16	2	3	5

Discussion

Chamberlin and Winship (1947), Dragstedt *et al.* (1947a), and Jackson (1949) have all described the anatomy of the vagal-nerve trunks in the region of the lower oesophagus. From these papers it would seem that, at the site of subdiaphragmatic vagotomy, only two nerve trunks were present in approximately 80% of 160 cadavers. From the results of our study, using the test here described, 14 of 16 cases had three or more nerve trunks capable, on stimulation, of causing gastric contraction (see Table). The significance of this difference in distribution is uncertain, but may be related to the fact that the small group we have studied were all patients with peptic ulceration. It now seems likely that the majority of cases presented for vagotomy have, at the subdiaphragmatic level, more than two motor nerve trunks to the stomach, and it is therefore possible that in the past any vagotomy in which only two trunks were removed was incomplete.

Dragstedt *et al.* (1947b) stated that recurrence or persistence of ulcer symptoms may occur if even a small vagus fibre to the stomach had been overlooked. They stated: "In man, apparently, the persistence of a small vagus fibre after section of two of the large vagal trunks permits the excessive night secretion characteristic of the ulcer patient. The remaining vagus fibre appears to be able to activate the whole glandular apparatus." They also stated that "where the vagotomy has been complete, there is, to date, no evidence of regeneration of the fibres in the vagus nerves." A possible explanation of Dragstedt's results is provided by the recent work of Murray and Thompson (1957a), who studied the results of incomplete nerve section in the autonomic nervous system. They showed that, if 90% of the total pre- or post-ganglionic sympathetic supply to an organ is cut, the remaining intact nerve fibres sprout and grow in such a way that complete recovery of function may take place within six weeks. With only 1% of the nerve fibres left in continuity, substantial recovery took place over several months. They have shown, too (Murray and Thompson, 1956b), that the vagus nerve can sprout.

It seems possible, therefore, that after incomplete vagotomy the remaining intact nerve fibres may sprout and within a few months the functional nerve supply to the stomach will have returned to a high level. This concept is supported by the incidence of positive insulin test meals in vagotomized patients. Lloyd Davies (1956) found that a marked response to hypoglycaemia with very high levels of free acid was found in 29% of 87 cases of vagotomy tested by the insulin test meal.

That the method described here is sensitive is shown by the smallness of the nerve trunks that it will detect. Fig. 6 shows a comparison of the normal nerve trunk with

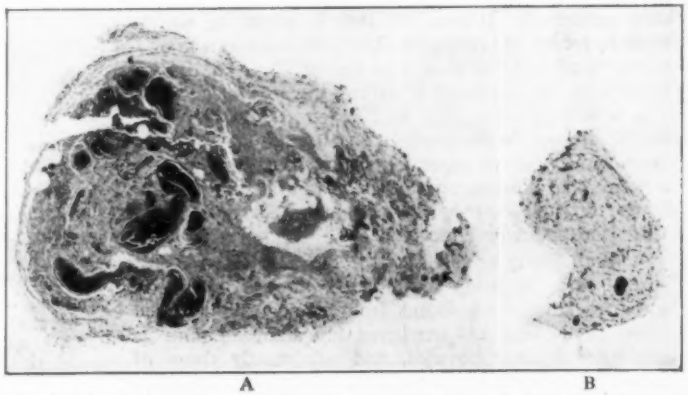

FIG. 6.—A: Section of a main posterior nerve trunk. B: Section of small nerve trunk (two bundles) which gave rise, on stimulation, to an increase of 1 cm. of water pressure. (Magnification in both instances ×21.)

a smaller trunk in transverse section which was found to be responsible for a rise of 1 cm. of water in gastric pressure on stimulation. If the motor and sensory nerves are randomly distributed in both these trunks then it appears that the method as at present used can detect a nerve trunk of about 1/50 the size of an average posterior vagus nerve.

Summary

A method is described which will detect the presence of even small vagal nerve trunks at the time of operation for vagotomy. If this method is used complete nerve-trunk section can be obtained.

We thank Professor Sir Lindor Brown for his advice; Dr. E. L. Harries for his help in the early stages of this work; Mr. H. Tennant and Mr. D. Green for their technical help; Spicers Ltd. for making the electrodes; Negretti and Zambra for making the pressure recorder; and Wm. Warne & Co. for making the gastric tube. We also thank the theatre sister and her staff of the West London Hospital for all their kind help in this work. This investigation has been made possible by the financial help of the Dan Mason Research Foundation of the West London Hospital Medical School.

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CEREBROSPINAL FLUID IN VARIOUS DISEASES

BY

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Greenfield and Carmichael in 1925 wrote a monograph on the cerebrospinal fluid (C.S.F.) which since that time has been one of the standard books of reference on this subject. The second part of that book was devoted to the results they found in various diseases seen during a period of five to six years. During the past 30 years innumerable papers and books have been written in which small series of results or even individual records were published. It was felt that it would be worth while to record the results of C.S.F. examinations in one neurological hospital over a period of 14 years, during which time the incidence of certain diseases has altered. The period chosen—1936 to 1949—was one in which almost all the fluids, totalling just under 12,000, were examined by one of us, and it also enabled us to obtain a period of follow-up should the need arise for revision of the original diagnosis, which had been determined when the patient left hospital.

A small group of diseases have been chosen for this special study as being common conditions, or because some variation was found from previously accepted views. The methods employed are standard ones as employed in this hospital, and are mostly those of Greenfield and Carmichael, with only minor variations.

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Results

Cerebral Tumour.—The results of the cell counts are given in Table I, and the protein levels are found in Table II. A

TABLE I.—*Cells in Cerebral Tumour per c.mm.*

Tumour	0–4	5–9	10–19	20–29	30–39	40–50	Over 50	Total Fluids
Cerebral glioma ..	299	10	7	4	5	4	6	335
Meningioma ..	136	4	—	—	—	—	1	141
Neurofibroma VIII ..	55	1	—	—	—	—	—	56
,, V ..	7	—	—	—	—	—	—	7
Brain-stem tumour ..	30	2	1	1	—	1	—	35
Cerebellar ,, ..	60	1	1	—	—	—	1	63
Intraventricular tumour	10	1	1	—	—	—	1	13
Choroid plexus ,, ..	10	—	—	—	—	1	—	11
Angioma	31	—	—	1	—	—	1	33
Pituitary tumour ..	61	7	1	—	—	—	—	69
Suprapituitary tumour	22	3	—	—	—	—	1	26
Secondary carcinoma ..	45	1	—	—	—	—	—	46

TABLE II.—*Protein in Cerebral Tumour in mg. per 100 ml.*

Tumour	0–40	45–95	103–295	300–495	500–1,000	Over 1,000	Total Fluids
Cerebral glioma ..	112	131	83	4	4	1	335
Meningioma ..	29	65	45	2	—	—	141
Neurofibroma VIII ..	—	11	27	12	5	1	56
,, V ..	—	1	5	1	—	—	7
Brain-stem tumour ..	12	14	9	—	—	—	35
Cerebellar ,, ..	26	20	15	1	1	—	63
Intraventricular tumour	7	1	4	1	—	—	13
Choroid plexus ,, ..	5	5	1	—	—	—	11
Angioma	13	9	10	1	—	—	33
Pituitary tumour ..	16	35	17	—	—	1	69
Suprapituitary tumour	8	13	5	—	—	—	26
Secondary carcinoma ..	14	21	8	2	—	1	46

total of 835 cases were examined, and all the results represent the findings at the first lumbar fluid examination. Greenfield and Carmichael record results in only 54 cases in their five-year period, so it will be seen that the incidence of such cases now treated in hospital has risen steeply. The features especially worthy of note are that, of the 835 cases, 766 (91.7%) showed no increase in cell count, and that any increase in cell count occurred chiefly in the glioma series. There were in all 69 cases showing a cell increase, and 36 of these (52.2%) were in cases of cerebral glioma, or 10.7% of all glioma cases. However, in only 242 cases (28.9%) was there a normal protein content. The cerebral glioma group showed a raised protein content in 66.5%, while in secondary carcinoma the figure was 69.6%, and in acoustic neurofibroma it was as high as 100%. The other tests employed did not show any features worthy of note.

It should be mentioned that care is needed if lumbar puncture is resorted to in cerebral tumour cases, and it should be performed only in selected patients and where neurosurgery is available.

Epilepsy.—The results are shown in Table III. As can be seen, in only 11 cases was the cell count raised, whereas the

TABLE III.—*Cells and Protein in Epilepsy*

Cells c.mm.	No. of Fluids	Protein (mg. 100 ml.)	No. of Fluids
0–4	893	0–40	559
5–9	7	45–70	290
10–19	3	75–100	53
20–30	1	105–150	2

protein was 70 mg./100 ml. or below in 93.9%. It was somewhat surprising to find that two cases had a protein above 100 mg./100 ml., and also that 25 cases showed a figure above 80 mg./100 ml.; but the records were carefully searched, and in no case had any of these patients returned to hospital for further investigation.

Multiple Sclerosis.—Some 690 cases were investigated, and Table IV shows the findings obtained. The cell count was normal in 589 cases (85.4%) and in only three patients was there a count above 50/c.mm. However, in six patients one or two polymorphs were present in the fluid, which is usually

said not to occur; also in eight patients large mononuclear cells were present, on one occasion numbering as many as 13%.

TABLE IV.—*Cells and Protein in Multiple Sclerosis*

Cells c.mm.	No. of Fluids	Protein (mg. 100 ml.)	No. of Fluids
0–4	589	0– 40	349
5–9	50	45– 70	254
10–19	34	75–100	62
20–29	8	105–120	12
30–39	6	125–150	7
40–49	—	155–200	3
50–82	3	205–300	3

The protein level was 100 mg./100 ml. or lower in 665 cases (96.4%), and in only 1.9% was a protein higher than 150 mg./100 ml. found. The clinical findings in all the cases showing a figure above 100 mg./100 ml. have been checked, and in all cases the diagnosis was accurate, being verified in many of them at necropsy and subsequent histology.

The Nonne-Apelt test was positive in 138 (20%) and the Pandy positive in 280 (40%). The Lange curve was normal or virtually normal in 481 (69.7%), a well-marked luetic curve was found in 125 (18.1%), and a paretic curve in 84 (12.2%). The Wassermann reaction was invariably negative.

Subacute Combined Degeneration.—Forty-one cases were examined, and in no case was the cell count abnormal; while the protein was normal in 20 cases, 100 mg. or less in 39, and in only two was it between 100 and 200 mg./100 ml. Globulin tests were positive on only 12 occasions, and a mild luetic Lange curve was obtained twice, while in 39 cases it was not abnormal.

Diabetic Neuritis.—No cell increase was noted in the 22 cases examined, and the protein was normal in 6, raised up to 100 mg./100 ml. in 19, between 100 and 200 mg./100 ml. in 2, and over 200 mg./100 ml. in only one case.

Infective Polyneuritis.—Table V shows the results found in 75 cases. The cell count was much more normal than

TABLE V.—*Cells and Protein in Polyneuritis*

Cells c.mm.	No. of Fluids	Protein (mg. 100 ml.)	No. of Fluids
0–4	66	0–40	16
5–10	6	45–100	22
11–100	2	105–200	19
Over 100	1	205–500	15
		505–1,000	2
		3,500	1

had been anticipated, but in more than half of the cases (37) the protein exceeded 100 mg./100 ml., and in all these the Nonne-Apelt and Pandy tests were positive. There was a coagulum in only five fluids, and in these the protein was 250 mg./100 ml. or more, while the fluid was coloured yellow in nine cases.

Syringomyelia.—Fluids from 78 cases have been examined, and in all except five a normal cell count was obtained, while 70 cases showed a protein below 100 mg./100 ml. The cells varied between 5 and 20 in the five abnormal cases, and the protein between 100 and 200 mg./100 ml. in seven cases, while one case had a protein of 240 mg./100 ml. No other abnormality was found.

Subdural Haematoma.—The fluids from 22 cases were examined, and in only four was there an increase of cells, on two occasions being between 5 and 10/c.mm. and in the other two cases being between 11 and 20/c.mm. The protein was normal in nine cases and between 45 and 100 mg./100 ml. in 13 patients. A slightly straw-coloured fluid was seen only twice.

Spinal Tumour.—The fluids from 238 cases were examined, and Table VI shows the results. Our findings were so similar in many ways to those of Greenfield and Carmichael that we have not classified them into intrathecal and extrathecal tumours. We have, however, found higher protein figures than they recorded, for, of the nine cases with figures above 3,000 mg./100 ml., two were as high as 4,000 mg./100 ml.

TABLE VI.—*Cells and Protein in Spinal Tumour*

Cells c.mm.	No. of Fluids	Protein (mg. 100 ml.)	No. of Fluids
0–4	202	0–40	41
5–9	19	45–100	68
10–19	6	105–200	42
20–29	4	205–500	43
30–49	2	505–1,000	13
50–100	4	1,005–3,000	22
More than 100	1	More than 3,000	9

Findings in Neurosyphilis

The findings in four groups only are given—meningo-vascular syphilis, tabes, G.P.I., and congenital syphilis. During the 14 years of this survey 770 cases falling into these four groups have been examined, but this number is relatively less than that of Greenfield and Carmichael, and agrees with our general view that tabes and G.P.I. are now relatively uncommon diseases.

Table VII shows the results in all these conditions. There are a few special features. The cell count was raised above

TABLE VII.—*Cells and Protein in Syphilis*

	Meningo-vascular	Tabes	G.P.I.	Congenital
Cells c.mm.:				
0–4	141 (64·7%)	154 (66·4%)	121 (54·5%)	40 (63·5%)
5–9	14	17	28	8
10–19 ..	16	16	20	5
20–39 ..	20	18	25	6
40–69 ..	14	13	16	2
70–100 ..	8	8	8	2
105–300 ..	5	6	4	—
Protein (mg./100 ml.):				
0–40 ..	62	63	55	30 (47·6%)
45–100 ..	120 (52·2%)	144 (59·3%)	124 (51·9%)	29 (46·0%)
105–150 ..	25	25	40	3
155–300 ..	16	9	18	1
305–500 ..	7	2	—	—
Over 1,000 ..	—	—	2	—
Lange curve:				
No change ..	59 (25·6%)	97 (40·9%)	35 (15·1%)	39 (61·9%)
Luetic	143 (62·2%)	108 (45·5%)	49 (21·1%)	10 (15·9%)
Paretic	28 (12·2%)	32 (13·5%)	148 (63·8%)	14 (22·2%)
Wassermann reaction:				
Positive in C.S.F. and blood ..	88 (39·3%)	147 (60·5%)	193 (81·4%)	13
Positive in C.S.F., negative in blood	14 (6·2%)	11 (4·5%)	6 (2·5%)	2
Negative in C.S.F., positive in blood ..	57 (25·4%)	26 (10·7%)	19 (8·0%)	19
Negative in C.S.F. and blood ..	43 (19·2%)	59 (24·3%)	19 (8·0%)	15
Positive in C.S.F. No blood ..	13 (5·8%)			4
Negative in C.S.F. No blood ..	9 (4·0%)			

100/c.mm. in only a very few cases, but polymorphs and large mononuclear cells were found in a number of fluids. In meningo-vascular disease there were 12 (5.5%) instances in which polymorphs were present, and these totalled 30% on two occasions. Large mononuclears were seen in 22 (10.1%) fluids, with a highest count of 20%. Polymorphs were present in fluids from tabetic patients on 21 (9.0%) occasions, and large mononuclear cells 28 times (12.1%). In G.P.I., polymorphs were seen in 32 fluids (14.4%), while large mononuclears were found in 46 (20.7%); and as many as half the total cell count has on occasion been composed of these types of cell.

The protein content had been above 300 mg./100 ml. on very few occasions, and in the vast majority of cases (92.5%) had been below 150 mg./100 ml.

The findings in the Lange and Wassermann tests were a little unexpected. A small but appreciable number of paretic curves were seen in both meningo-vascular syphilis and in tabes, while slightly more luetic curves were seen in

G.P.I. There were a relatively large number of negative Wassermann reactions in both blood and C.S.F. in meningovascular syphilis, and certainly more (8%) than were expected in G.P.I. There was also 8% of cases of G.P.I. in which, although the blood Wassermann reaction was positive, the C.S.F. Wassermann reaction was negative. This is unexpected, as it is usually thought that the Wassermann reaction is almost always positive in the C.S.F. The wide variations in the findings in congenital syphilis were not unexpected.

Other Neurological Disorders

The findings in some other neurological disorders investigated were in general agreement with those already published in standard textbooks, but one or two points might be mentioned. The C.S.F.s from 29 patients with a cerebral abscess have been examined, and only seven of them were even faintly turbid. In eight the cell count was normal, while, of the remainder, 13 showed between 5 and 100 cells; polymorphonuclear leucocytes were seen in only 19 of the 29 fluids. The protein was normal on 10 occasions and less than 200 mg./100 ml. in all except three fluids. No other significant features were noted.

Fluids from 10 patients with a cerebral tuberculoma diagnosed during life were examined, and all seven who died were seen in the pre-streptomycin era. The only significant features that emerged from the examinations made in this very small series was that the pre-operative fluid may contain neither an increased cell count nor a raised protein content.

Many other comments could be made, but the evidence for these is slight; one remark can, however, be added—namely, that there was found to be a rather wider variation in the results than one is commonly inclined to allow; and one lesson that we have personally learned is to be rather less dogmatic than had previously been our custom.

Summary

An analysis of the results obtained from the examination of nearly 12,000 C.S.F.s from various neurological disorders has been made.

The C.S.F. in 835 cases of all types of cerebral tumour has shown a cell increase in only 8.3% of cases, but a protein increase in 71.1%, cerebral glioma giving figures of 10.7% and 66.5% respectively. Fluids from cases of neurofibromata—whether on the fifth or the eighth cranial nerve—contained a protein content raised above the normal.

In 6.1% of the cases of epilepsy the fluid protein was raised above 70 mg./100 ml., and in two cases a figure of over 100 mg./100 ml. was obtained.

The findings in 690 patients with multiple sclerosis are discussed, and in 1.9% of cases—many verified at necropsy—there was a protein content in the fluid above 150 mg./100 ml.

Unexpected results were not found in subacute combined degeneration, diabetic neuritis, infective polyneuritis, syringomyelia, or subdural haematoma.

The results of fluid examination in 238 cases of spinal tumour were in conformity with previous reports, but figures for protein as high as 4,000 mg./100 ml. were found.

The cases of neurosyphilis examined (770) are fewer than expected, but the findings, apart from the results of the Lange and Wassermann tests, were similar to those previously recorded. The most unexpected finding was an occasional negative fluid Wassermann reaction in G.P.I.

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BRONCHITIS MORTALITY RATES IN ENGLAND AND WALES AND IN DENMARK

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In England and Wales bronchitis is recorded as the cause of death in over 25,000 people every year, and it accounts for half the deaths due to respiratory diseases and 5% of deaths due to all causes. The recorded mortality rates in other European countries and in the United States of America are much lower. In this paper the causes of death in England and Wales and in Denmark are analysed and compared, and some factors are considered which might be responsible for the recorded excess mortality from bronchitis in England and Wales.

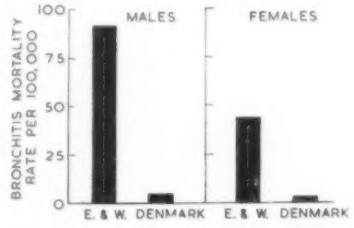

FIG. 1.—Mortality rates per 100,000 from bronchitis in England and Wales (E. & W.) and in Denmark: average for 1951–5. Bronchitis includes: acute bronchitis (500); bronchitis, unqualified (501); chronic bronchitis (502), including bronchitis with emphysema (502.0) and other (502.1). The International List numbers are given in parentheses.

The difference in mortality rates for bronchitis in the two countries obtained from the Registrar-General's Statistical Review and the Causes of Death in the Kingdom of Denmark is shown in Fig. 1.

Choice of Cause of Death from Death Certificates

The current form of death certificate used in England and Wales, which has space for recording the underlying cause, complications, and contributory causes, was introduced in 1927. For thirteen years the selection of the cause of death for tabulation from certificates giving multiple causes was governed by a set of rules which gave priority to certain causes. For example, any definite disease of the kidneys or heart (and this included myocardial degeneration) was preferred to any respiratory disease. In 1940 the International Statistical Classification of Diseases, Injuries, and Causes of Death was adopted, and this lays down that, with certain exceptions, the cause of death for tabulation shall be that which the certifier records as the underlying cause.

The effect of this change in selection procedure on bronchitis mortality rates for men in England and Wales in 1939 was calculated by Schilling and Goodman (1951). They found that by applying the 1940 method of classification to the 1939 figures it increased the age specific mortality rates from bronchitis by the following amounts: 25–34 years, 31%; 35–44 years, 48%; 45–54 years, 71%; 55–64 years, 97%; and 65–69 years, 114%.

Since 1951 Denmark has also used both the International Certificate of Cause of Death and the International Statistical Classification of Diseases, Injuries, and Causes of

Death, but for chronic bronchitis the special rules given below are applied (Lindhardt—personal communication):

1. Whenever chronic bronchitis appears together with arteriosclerotic heart disease, including coronary disease (420), other myocardial degeneration (422), functional disease of heart (433), and other and unspecified diseases of heart (434), they—the heart diseases—will be coded as the underlying cause.

2. Whenever chronic bronchitis appears together with bronchiectasis (526) the latter will be coded as the underlying cause; whenever chronic bronchitis appears together with lobar pneumonia (490) the latter will be coded as the underlying cause.

3. Chronic bronchitis together with asthma bronchiale (241) is coded as chronic bronchitis (502) unless the patient died in status asthmaticus.

4. Until 1955 chronic bronchitis together with bronchopneumonia was coded as bronchopneumonia (491), but now this combination is coded as chronic bronchitis (502).

These Danish rules, which are in essence the same as those used in England and Wales before 1940, would only have the effect of reducing the bronchitis mortality rates if another cause of death was often combined with chronic bronchitis. The analysis of multiple causes of death which was undertaken by the Registrar-General on a sample of death certificates in 1951 (Registrar-General, 1951) shows that bronchitis often occurs in combination with other diagnoses. If the Danish rules of selection are applied to this sample of English certificates many cases tabulated as chronic bronchitis would be ascribed to cardiovascular causes. This would reduce the total bronchitis mortality rate of this sample by approximately 45%. The same procedure cannot be applied to Danish death certificates because multiple causes of death are not tabulated, but the death rates from causes to which cases of bronchitis in Denmark might be ascribed according to their rules are given in Table I with the corresponding rates for England and Wales.

TABLE I.—*Crude Mortality Rates per* 100,000 (*Both Sexes*, 1954) *for Various Groups of Diseases to which Cases of Bronchitis Might be Ascribed in Denmark, Compared with Rates in England and Wales*

Causes of Death	International Number	Crude Death Rate	
		England and Wales (Pop. 44,274,000)	Denmark (Pop. 4,405,700)
Acute bronchitis	500	7	2
Bronchitis, unqualified	501	5	0
Chronic bronchitis	502	46	4
Asthma bronchiale	241	6	1
Arteriosclerotic heart disease, including coronary disease	420	151	150
Other myocardial degeneration	422	145	50
Functional disease of heart	433	6	6
Other and unspecified diseases of heart	434	11	28
Lobar pneumonia	490	7	3
Bronchopneumonia	491	30	15
Bronchiectasis	526	4	2
Total		418	261

There is an excess mortality in England and Wales for all the respiratory and cardiac conditions recorded in Table I, except "Other and unspecified disease of heart" (434). Even if the whole of the Danish excess in this group were due to differences in the diagnosis and assignment of cases of bronchitis, which is unlikely, it could not explain the tenfold excess in bronchitis mortality in England and Wales.

In contrast to the large difference in mortality from chronic bronchitis, there is a marked similarity in the rates for diseases, such as congenital malformations and neoplasms, in which a greater uniformity of diagnostic habit is to be expected (Table II).

It is likely that the different death rates for the two countries cannot be explained wholly by different methods of bookkeeping and that there is a real excess of deaths from chronic bronchitis in England and Wales. Some causes of this excess are considered.

TABLE II.—*Crude Death Rates per* 100,000 (*Both Sexes*, 1954) *in Certain Groups of Diseases in England and Wales and in Denmark*

Causes of Death	International Number	Crude Death Rate	
		England and Wales	Denmark
Neoplasms	140–239	207	198
Diseases of the genito-urinary system	590–637	28	31
Diseases and complications of pregnancy, childbirth, and the puerperium	640–689	5*	6*
Congenital malformations	750–759	10	9

* Rates per 100,000 women aged 15–44.

Age and Sex.—The greater number of deaths from bronchitis in England and Wales is not due to difference in age and sex distribution. Of the deaths from chronic bronchitis, 95% occur over the age of 45. In England and Wales this age group comprises 36% of the total population, compared with 32% in Denmark, and 47% are male compared with 48% in Denmark. The age specific death rates for males and females in the two countries (Table III) show that the excess mortality in England and Wales occurs at all ages for both sexes. It will also be seen that the great predominance of male deaths in England and Wales is much less marked in Denmark.

TABLE III.—*Age and Sex Specific Death Rates per* 100,000 (1954) *for Chronic Bronchitis* (502)

Age	Population in 1,000's		Total Deaths		Death Rate	
	E. and W.	Denmark	E. and W.	Denmark	E. and W.	Denmark
Males						
0–14	5,092	600	21	2	0	0
15–44	9,002	909	200	4	2	0
45–54	3,863	274	1,204	8	39	3
55–64	2,106	205	3,437	20	163	10
65–74	1,380	134	5,331	23	386	17
75+	645	65	4,374	48	678	74
Females						
0–14	4,863	571	14	0	0	0
15–44	9,236	915	74	3	1	0
45–54	3,222	285	245	2	8	1
55–64	2,633	223	683	10	26	4
65–74	1,948	149	1,708	13	88	9
75+	1,084	74	2,995	53	76	71

Social Class.—The social-class gradient of mortality from chronic bronchitis in this country cannot be compared directly with Danish figures, as these are not broken down by social class. However, a comparison, related to social class, can be made in the level and distribution of the national income per head (United Nations, 1952). In both countries the average income is within the range of U.S. $600–699 and the distribution is about the same. The proportion of the total national income received by the richest tenth in the United Kingdom (after income tax) is 26% and in Denmark 29%. The proportion of the total received by the poorest half in the United Kingdom is 30%, compared with 23% in Denmark. Thus it is unlikely that differences in the standard of living are a major factor in the different bronchitis mortality rates.

Urban and Rural Residence.—The mortality rates from bronchitis according to residence are shown in Table IV. In England and Wales the well-known urban–rural gradient in bronchitis mortality is clearly shown. In the Danish figures there is, by contrast, a slightly higher mortality in the rural districts. Air pollution has been suggested as one factor responsible for the urban–rural gradient in England and Wales. Campbell and Clemmesen (1956) made a comparative study of air pollution in the two countries and concluded that Copenhagen, the most industrialized city in Denmark, was polluted to about the same extent as an English rural town. However, from Table IV it will be seen that the mortality rates for bronchitis in all areas in Denmark are lower than for rural districts in England and Wales. It is therefore unlikely that the difference in the mortality rates could be due to differences in air pollution alone.

TABLE IV.—*Crude Death Rates per* 100,000 (*Both Sexes*, 1954) *from Bronchitis* (500–502) *by Residence*

England and Wales			Denmark		
Regions	Population in 1,000's	Death Rate	Regions	Population in 1,000's	Death Rate
Conurbations ..	16,894	65			
Urban area with population of 100,000 and over	5,851	61	Copenhagen ..	776	6
Urban area with population of 50,000 and under 100,000	3,391	58	Provincial towns, including Frederiksberg	1,292	5
Rural districts ..	8,610	42	Rural districts, including Gentofte	2,357	7

Tobacco Consumption.—A comparison of the average weight of tobacco consumed per head per year in England and Wales and in Denmark, and the proportion of this that is smoked as cigarettes, are given in Fig. 2. The total annual

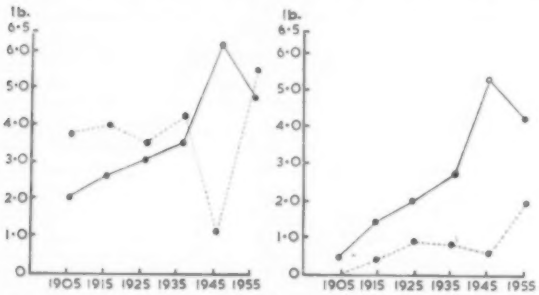

FIG. 2.—Tobacco consumption in England and Wales (———) and Denmark (- - - -), 1905–55. Left: Total annual consumption of tobacco (unmanufactured) per person, in pounds. Right: annual tobacco consumption as cigarettes per person, in pounds.

consumption per head has been lower in this country than in Denmark except for the war years. However, the amount smoked as cigarettes has always been more than twice the Danish figures. Oswald *et al.* (1953), Palmer (1954), and Ogilvie and Newell (1957) have shown that the prevalence of bronchitic symptoms is related to cigarette-smoking. The national smoking habits may therefore contribute to the bronchitis mortality excess recorded in England and Wales.

Climatic Conditions.—In England and Wales the mean annual rainfall is a little greater than in Denmark and the winter temperatures are a little higher. However, both countries lie in the same belts of mean annual temperature (7.22–10.00° C.), mean atmospheric pressure (754.4–759.5 mm.), and wind direction. Thus climate alone cannot directly contribute to the excess in England and Wales.

Summary and Conclusion

A fifteenfold excess of mortality from bronchitis is recorded in England and Wales compared with Denmark. Both countries use the International Certificate of Cause of Death and the International Statistical Classification of Diseases, Injuries, and Causes of Death. However, differences in the method of selecting causes of death for statistical purposes, when multiple causes are given, still occur: these could account for as much as half the excess mortality in England and Wales. Possible differences in diagnostic habits may contribute to the remaining excess but do not appear to explain it. The cigarette consumption of England and Wales is twice that of Denmark and might also contribute to this excess; but when considered separately the differences in the age distribution, social class, climate, and atmosphere pollution of the two countries do not appear to be important factors.

Within the strict limits imposed by differences in method of compiling the death rates, it would appear that there is a real excess of the disease labelled bronchitis in England and Wales, compared with Denmark; but the confirmation of this difference and the elucidation of its causes are likely to result only from comparative field surveys in the two countries.

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ANTIBODY RESPONSES TO BRITISH POLIOMYELITIS VACCINE OF CHILDREN WITH NATURALLY OCCURRING ANTIBODY

BY

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The results have already been reported of a study of the antigenic activity of British poliomyelitis vaccine in a group of children who, at the time of their first injection of vaccine, had no antibodies to any of the three types of poliomyelitis virus (Medical Research Council, 1957a). In selecting this group the sera of a number of children in five different areas were tested, and, although those who were shown to have antibodies to one or more types were excluded from the Council's study, they were nevertheless injected with poliomyelitis vaccine. The antibody responses of some of these children were investigated and the results are reported here.

Titration of Sera

Sera from 254 London and Manchester children, aged from 1 to 9 years, were obtained before giving two intramuscular injections of formalinized poliomyelitis vaccine (Glaxo) four weeks apart. Samples of sera were also obtained 14 days after the second injection. All sera were titrated for neutralizing antibody to the three types of poliomyelitis virus by the method used routinely in the Biological Standards Control Laboratory (Medical Research Council, 1957a). In this method, serum-virus mixtures are held at 37° C. for three hours before being added to cultures of monkey-kidney cells, and the titres (PD_{50}) expressed as the dilution of serum in the serum-virus mixture and not as the initial serum dilution. The three virus strains used in the neutralization tests were the same as those employed in the manufacture of British vaccine—namely, the attenuated Brunenders for type 1, MEF-1 for type 2, and Saukett for type 3. In three cases one type was omitted because of insufficient serum. Children whose serum at a dilution of 1/8 did not inhibit any one of the poliomyelitis viruses were regarded as negative so far as that type was concerned. The sera of those who did not produce this titre after vaccination were also tested at a dilution of 1/4.

Results

Of the 254 sera taken before vaccination, 68 had no antibodies to any of the three types, and 64 of these were included in the triple-negative study already reported (Medical Research Council, 1957a). Of the remaining 186 sera, 55 contained antibodies to one type only, 67 to two types, and 64 to three types. The types were fairly evenly distributed throughout the group, 120 having antibodies to type 1, 122 to type 2, and 141 to type 3.

The response of the children with pre-existing antibody to each component of the poliomyelitis vaccine is given in the chart with reference to the level of pre-existing homologous antibody. It is compared with the response of the 68 triple-negative children whose sera were titrated in the same laboratory and by the same method. As can be seen, there was a great variation in the antibody titre produced in children without initial homologous antibody both in those who were triple negative and in those with heterologous antibody. Two children in the triple-negative and one in the heterologous antibody group failed to produce antibody to type 1. None of the children in either group failed to produce some detectable antibody to types 2 and 3.

In those children with pre-existing homologous antibody to the type being investigated, the levels produced were very much higher, only one failing to produce a titre of 512 to type 1 and two to each of the other types.

The effect of heterologous antibody on the response is given in the Table. As an epidemic of type 1 poliomyelitis was occurring in the Manchester area during the vaccination programme, it was concluded that the high titres (8,192 and over)—all of which were in children from that area—were due to infection, and these were excluded from the analysis, as was done in the Medical Research Council report. The geometric mean titres of the children with heterologous antibody to the types indicated are compared with those obtained in triple-negative children. Although the groups were small, it would appear that with type 1 virus the presence of type 2 antibody, but not type 3, increased the level of antibody produced; with type 2, pre-existing antibody to either type 1 or type 3 produced this effect, whereas with type 3 enhancement was evident only when both heterologous antibodies were present.

Effect of Pre-existing Heterologous Antibody on the Response to Poliomyelitis Vaccine of Children with No Homologous Antibody

Type of Test Virus	Geometric Mean Titre after Vaccination of Sera from Children with Pre-existing Antibody to:				
	No Type	Type 1	Type 2	Type 3	Both Heterologous Types
1	79 (68)	—	575 (13)	68 (25)	132 (24)
2	245 (67)	818 (15)	—	682 (25)	960 (24)
3	113 (68)	94 (15)	120 (13)	—	224 (17)

Figures in parentheses indicate number of children in each group.

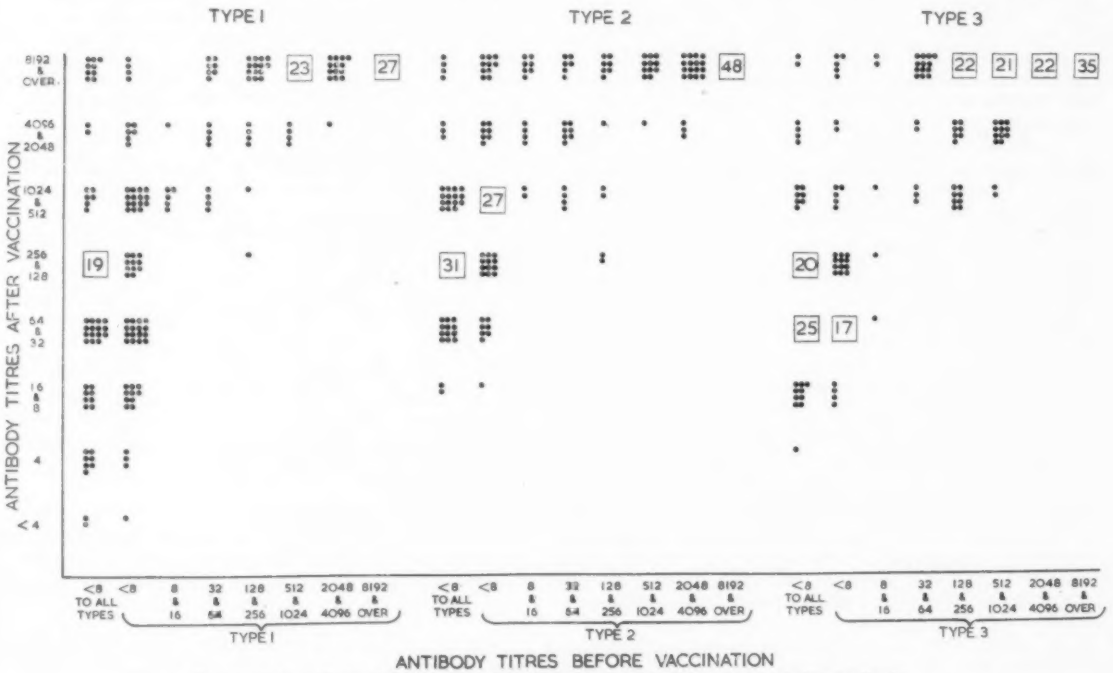
Conclusions

The results reported here follow the same pattern as those noted in triple-negative children, all except one child responding to all three components of the vaccine, including those types in which they were deficient before vaccination. In those with pre-existing homologous antibody a "booster" type of response was obtained similar to that which occurs in children with vaccine-induced antibody (Medical Research Council, 1957b).

The type 1 component of the British vaccine is prepared from the attenuated Brunenders strain instead of from the more virulent Mahoney strain preferred in North America. With the vaccine used in the United States, Salk (1956) has shown that the presence of pre-existing heterologous antibody may affect the response to any given virus types. The results noted here in children with different poliomyelitis antibody spectra before vaccination suggest that the Brunenders component of the British vaccine behaves in the same way, as the response to it is similarly enhanced by the presence of pre-existing type 2 antibody.

Summary

The response to the British poliomyelitis vaccine in 186 children with naturally occurring antibody was investigated. The results indicated that children with



Response to poliomyelitis vaccine of children with and without pre-existing antibody.

pre-existing heterologous antibody may show an increased response to a given type, while those with pre-existing homologous antibody give a "booster" response.

Thanks are due to Dr. J. A. Dudgeon, Dr. J. C. W. MacFarlane, Dr. D. O'Brien, and Dr. A. M. Peach (London), and to Dr. P. B. Stones and the medical staff of the Health Department (Manchester), who were responsible for immunizing and collecting sera from the children.

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HAEMOLYTIC ANAEMIA FOLLOWING THROMBOCYTOPENIC PURPURA

BY

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Primary thrombocytopenic purpura associated with red-cell sensitization was originally described by Evans *et al.* (1951). In their group of five patients presenting with primary thrombocytopenic purpura together with evidence of red-cell sensitization, one developed a haemolytic anaemia following splenectomy.

In the case described below an acute haemolytic anaemia developed after apparent spontaneous recovery from primary thrombocytopenic purpura.

Case Report

A 58-year-old man was referred to the dermatological out-patient department with varicose eczema, which had been present for 10 years. Four months later extensive purpura appeared on the legs, thighs, and trunk. Inquiry elicited that similar attacks with occasional epistaxis had occurred at irregular intervals over the preceding 10 years. He had taken no drugs likely to produce haematological effects.

Examination on January 3, 1956, revealed a heavily built man with healed varicose ulceration covering an extensive area of both legs. There was a purpuric eruption over the legs, thighs, and trunk. Neither the spleen nor the liver was palpable.

Investigation showed: Haemoglobin, 13.3 g./100 ml., red blood cells, 4,500,000/c.mm.; platelets, 15,000/c.mm.; white cells 7,000/c.mm., with a normal differential count. Reticulocytes were less than 1%, and the bleeding-time was nine minutes. Examination of the marrow showed some maturation arrest of the thrombocytic series. The tourniquet capillary fragility test was positive, and capillary microscopy showed tortuosity and varied calibre, with defective contractility of the capillaries on trauma. The patient was group O, rhesus negative. Serial dilution anti-human-globulin test was positive to a titre of 128, with pan- and auto-agglutinins in saline and albumin at 4° C. No rhesus, Kell, or platelet antibodies active at 37° C. were detected.

Five months later he was admitted to a medical ward with symptoms suggestive of coronary thrombosis. Examination showed that the purpura had cleared and there were no abnormal findings on examination of the cardiovascular system.

In view of the history of purpura the haematological investigations were repeated on June 6: haemoglobin, 12.6 g./100 ml.; red blood cells, 3,800,000/c.mm.; platelets, 200,000/c.mm.; white blood cells 2,000/c.mm. (band cells, 2%, neutrophil polymorphs 40%, eosinophil polymorphs 16%, basophils 0.1%, lymphocytes 20%, and monocytes 22%).

Over the next three weeks the haemoglobin fell to 9.8 g./100 ml., but the platelet and white-cell counts remained constant. As the patient was suspected of having sustained a small coronary thrombosis without electrocardiographic changes he was discharged home after three weeks' bed rest. In view of his apparent recovery from primary thrombocytopenic purpura and the leucopenia which had developed, it was decided to keep him under observation.

Three months later he was readmitted because of rapidly increasing anaemia. Examination showed marked pallor with mild icterus. The spleen was just palpable. Haemoglobin, 8 g./100 ml.; red blood cells, 2,420,000/c.mm.; platelets, 250,000/c.mm.; white blood cells 3,000/c.mm. (neutrophil polymorphs 54%, eosinophil polymorphs 2%, lymphocytes 40%, monocytes 4%). The reticulocyte count was 18% and the erythrocyte sedimentation rate was 138 mm. in the first hour (Westergren). The urine contained excess urobilin and urobilinogen, and the total faecal urobilinogen was 731 mg./100 g. of faeces.

Marrow examination showed greater activity of normoblasts and macronormoblasts than noted previously. Haemolysis continued, and three weeks later the haemoglobin was 5.6 g./100 ml. and the red cells numbered 1,670,000 per c.mm. The direct antiglobulin test was positive in serial dilution. The antibody coating of the erythrocytes appeared to be a mixture of gamma- and not-gamma-globulins. The acid haemolysin test was negative; there was a strong auto-agglutinin active at 37° C., 20° C., and 4° C., and a pan-agglutinin at 4° C. active in saline and albumin.

The direct antiglobulin test on the platelets was negative: platelet antibodies were not demonstrable by the methods of Stefanini *et al.* (1953) and Dausset *et al.* (1952), or by the indirect antiglobulin test. No antibodies could be eluted from the red cells after elution at 56° C. for 10 minutes. A preparation of stroma from three-times-washed red blood cells, eluted at 56° C. with 8% albumin, reacted with all group O cells tested.

At this point treatment with corticotrophin was begun, and was followed by a rapid rise in haemoglobin to 12.4 g./100 ml., and in red blood cells to 3,850,000/c.mm. The platelet count rose to 620,000/c.mm., and the white cell count to 8,000/c.mm. (see Table). Maintenance therapy with prednisone was continued until the time of report.

Date	Hb. (g. 100 ml.)	R.B.C. (10^6 c.mm.)	W.B.C. per c.mm.	Retics.	Platelets Lempert per c.mm.	Direct Anti-globulin Test
3/1/56	13·3	4·5	7,000	1%	15,000	+
6/6/56	12·6	3·8	2,000		200,000	
25/6/56 ..	10·4	3·01	2,000		200,000	
3/10/56 ..	8·0	2·42	3,000	18%	250,000	
23/10/56 ..	5·6	1·67	3,400		570,000	
Corticotrophin, 120 u. daily						
29/10/56 ..	8·3	2·55	4,000	20%	620,000	+
7/11/56 ..	12·4	3·85	8,000	18%		
Prednisone, 30 mg. daily						
22/11/56 ..	13·9	4·25	7,000	2%	130,000	
6/12/56 ..	13·3	3·8	8,000		280,000	
Prednisone, 20 mg. daily						
20/12/56 ..	14·8	4·8	—	4%	280,000	
3/1/57	15·0	5·0	9,000	4%	300,000	
23/1/57	Prednisone, 10 mg. daily					
24/1/57 ..	14·5	4·4	8,000		340,000	
Prednisone 5 mg. daily						
21/2/57 ..	14·8	4·5	6,000	3%	400,000	
29/12/57 ..	14·8	4·8	6,000	1%	190,000	+

The antiglobulin test in serial dilution remained strongly positive after treatment was started. Further attempts to demonstrate platelet antibodies were unsuccessful.

Discussion

The association of a low platelet count with evidence of red-cell sensitization led Evans *et al.* (1951) to suggest the existence of immuno-thrombocytopenic purpura. Dausset

et al. (1952), Miescher *et al.* (1952), Stefanini *et al.* (1953), Harrington *et al.* (1953), Kissmeyer-Neilsen (1953), Tutein Nolthenius *et al.* (1953), Sauer and van Loghem (1954), Jaeger-Draafsel *et al.* (1956), and Tullis (1953) have developed techniques for the detection of platelet antibodies, and have applied these techniques to the study of platelet antibodies in thrombocytopenic purpura. In the cases in which Dausset *et al.* (1952) found platelet antibodies there had been a history of concomitant disease, or of previous transfusions which had complicated the interpretation of the platelet antibody.

In the above case there seems to have been three phases of destruction or suppression of the cellular elements of the blood. The patient presented with an illness which was indistinguishable from thrombocytopenic purpura. Spontaneous recovery from this ensued, and was followed by a period of symptomless leucopenia. Subsequently he developed the haemolytic anaemia which had been anticipated from the inception of his illness because of the strongly positive Coombs test.

When the patient was first seen the platelet count was too low for a direct antiglobulin test to be performed on the platelets according to the technique of Nelken and Gurevitch (1956). Following the development of the haemolytic anaemia the direct antiglobulin test was performed on the platelets on several occasions with negative results, and the serum was not found to contain a complete or an incomplete platelet antibody. Despite this, wide variations in the platelet count have occurred.

Evans *et al.* (1951) claimed that the immune globulin coating of the red cell was the critical factor for haemolysis. The fact that a strongly positive antiglobulin reaction was observed before the onset of haemolysis and during the phase of recovery does not support this view. This is borne out in other cases by the failure of the antiglobulin reaction to become negative even after long periods of treatment with steroid hormones and despite the successful control of the haemolytic process (Dameshek and Reeves, 1956). While "anti-red-cell" antibody production has not been suppressed the abnormal destruction of the sensitized red cells has been arrested by steroid therapy.

The period between the appearance of thrombocytopenia and haemolytic anaemia seems to have been characterized by leucopenia when the other formed elements were not affected. The process of cell destruction seems to have affected one series at a time and does not appear to have been associated with a specific antibody.

The strongly positive antiglobulin test, together with the asynchronous depression of the three formed elements of the blood, makes it unlikely that these features of the patient's illness result from hypersplenism alone.

The possibility that this patient had lupus erythematosus, as in the cases reported by Dameshek and Reeves (1956), was considered. Repeated attempts to demonstrate the L.E. cell phenomenon failed, but, as these workers showed, this phenomenon may not appear until splenectomy has been performed.

Summary

A case is described in which there was spontaneous recovery from idiopathic thrombocytopenic purpura, followed after an interval of several months by the development of an acquired haemolytic anaemia.

The significance of a strongly positive antiglobulin test accompanying thrombocytopenic purpura is discussed.

We are indebted to Dr. E. K. Blackburn for haematological investigations and Dr. A. E. Mourant and Mr. I. Dunsford for helpful criticisms.

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GREASE-GUN INJURY TO THE HAND

VALUE OF EARLY TREATMENT

BY

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Increasing automation and speed in the lubrication services available for motor-cars is making injury by high-pressure injection of grease into the hand and fingers less uncommon. When it occurs a distressing and crippling reaction ensues. References to the injury are becoming more numerous; Mason and Queen (1941) recorded two cases and brought an interesting literature together, and more recently Rank and Wakefield (1953) and Bunnell (1956) have brought it to some prominence in textbook form.

The air-compressors which are used to provide the force behind the grease have an output, in most garages, of 100–200 lb. per square inch (7–14 kg. per square cm.), and, while this in itself may not be sufficient to cause penetration, the pressure of the grease coming through the small orifice of the grease-gun may be anything from three to twenty times as great (600 lb. per square inch (42 kg. per square cm.) seems to be an average figure). Grease nipples on the steering connecting rods or on the propeller shafts have the annoying habit of turning away as soon as pressure is applied (the owner who carries out such servicing by himself appreciates this through the loss of skin from knuckles). It is often necessary to steady the nipple with the free hand, but if the gun slips and high-pressure lubrication is in use, the reaction of the finger on the trigger is not in time to avert the injection of grease or oil into the other hand or fingers which the nozzle may come up against.

From the moment of injury the stages of surgical pathology and the clinical features follow in dreadful succession. Owing to the unyielding attachment of skin to deep fascia by the fibrous septa (also well known for the anatomical basis of the aetiology of blisters), the part is tightly distended by the grease, some of which may be forced along those fascial compartments occupied by digital nerves and vessels. Pressure necrosis and gangrene may therefore occur. Tenseness, numbness, and pallor are present, and through a small pin-point or laceration grease may ooze or be expressed.

It is the delay in obtaining an immediate release of the entrapped grease under tension which results in the gangrene and loss of the part or, if not this, the development of a chronic granuloma (an oleoma). The chemical properties of the grease (so often a soap or paraffin salt, with addition of lime salts) set up an inflammatory response with islands of grease surrounded by fibrous tissue, foreign-body giant cells, and lymphocytes. Superadded infection is common. Function is lost.

Lastly, the development of contractures, ulcers, recurrent infection, even elephantiasis and cancer, seems to be the outlook over the years.

The following case report is a good illustration of the problem and the treatment, particularly the early treatment initiated by the patient and continued immediately and more efficiently by the doctor, who had appreciated the need for this from a previous unhappy experience. The operation in hospital shows how difficult the problem is known to become after an interval, with sequestration of the grease and massive fibrous response and tethering of digital nerves. Fortunately amputation was not indicated here.

Case Report

The patient was a service-bay mechanic aged 36. While greasing a motor-car with a high-pressure grease-gun the nozzle slipped off a nipple and grease was injected into the palm of the left hand (placed close to greasing-point for steadiness). At once he squeezed out some of the grease, and went to his doctor, who opened up the wound immediately and expressed a further amount. The wound healed, but the swelling caused by the injury increased, with concomitant pain and limitation of finger movements. He was aware of something fluctuant in the swelling. A few days before admission to hospital, one month after the injury, it became more tender and some "pus" exuded from one place.

Grease-gun injury, showing the thickening of finger and palm, with sinuses.

Examination of the left hand showed a tense, tender, non-fluctuant swelling of the distal part of the palm particularly, including the proximal part of the middle finger, which was stiff. At the base of the finger were two small sinuses, but nothing could be expressed from them (see Fig.). *X*-ray examination showed the soft-tissue swelling and no bone disease.

Before operation an inquiry was made of the manufacturers concerning the constituents and solvents of the grease. The reply stated that there were two main constituents—the fat portion, soluble in ether, and calcium, added as lime, and for the removal of which little could be suggested.

Operation.—With the use of a "bloodless field" technique, incisions were made using convenient skin creases of the palm and at the base of the middle finger, with an extension along the radial side of the proximal phalanx in front of the position of the neurovascular bundle. Flaps were turned back, and soon about 2 dr. (7 ml.) of unaltered golden grease escaped from a cavity in the extensive fibrous thickening of the palmar fascia. This thick layer of fibrous tissue was carefully pared away in piecemeal fashion, revealing many small cavities containing either grease or what appeared to be thick white pus. On the radial side of the base of the middle finger a larger cavity containing pus adjacent to the flexor tendon sheath was found. A sample of the pus was taken for examination and culture, together with a portion of the affected fascia for histology. The wound was closed with interrupted silk sutures. The hand was elevated for nursing.

Examination and culture of the "pus" showed no bacteria and there was no growth. The substance was not, in fact, pus, but was found to consist of minute droplets of emulsified grease.

Histology of the palmar fascia showed a well-marked chronic inflammatory reaction with foreign-body giant cells in fair numbers.

The wound was slow to heal, but movements of the fingers improved early. There was some loss of sensation on the ulnar aspect and pulp of the middle finger. The wound remained tender, and movement did not return as fully as hoped for, but three months later, after return to work, a more rapid improvement took place. Now, over two years since the injury, there has been no loss of time from work, and the fingers and hand are practically normal in function, though some numbness of the pulp of the middle finger still remains.

Summary

An instance of the increasingly common grease-gun injury is recorded, particularly because the crippling effect of such a foreign material had largely been prevented by the immediate step of incision and expression by the patient's own doctor. Though the appearance of the affected hand was still sinister afterwards, a good result was achieved after operative removal of the rest of the grease—some of which had undergone emulsification and so mimicked creamy pus. The surgical pathology and anatomy are discussed briefly.

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Medical Memoranda

Myasthenia Gravis Occurring in Association with a Malignant Thymic Tumour

Until recently it was believed that thymic tumours associated with myasthenia gravis were benign (Bratton, 1948). There have, however, been numerous reports of the invasive character of these tumours (Claggett and Eaton, 1943; Murray and McDonald, 1945; Reid and Marcus, 1949). Some instances of implantation on to pleural surfaces and a few of lymphogenous and haematogenous spread have been reported (Keynes, 1946, 1955; Tajima, 1952). In the series of thymic tumours reported by Scybold *et al.* (1950), although many were invasive in character, embolic metastasis was not found.

Some 75% of patients having tumours develop or already suffer from myasthenia gravis. The remaining tumours unassociated with this disease are often described as highly malignant, and considerable doubt has been expressed about the true source of some of these.

Case Report

An electrician, aged 41, first complained of hoarseness of voice and mild dysphagia in July, 1955. These symptoms were accompanied by a sore throat, and became worse after carrying on a conversation. In September he was seen by an E.N.T. surgeon, and an indirect laryngoscopy was performed. In December a barium swallow was carried out, and after this he was reassured and discharged.

In February, 1956, he was referred to one of us (P. E.) because he developed a mild cough. There were no physical signs in his chest. *X*-ray films of his chest taken in the postero-anterior and lateral positions showed a homogeneous opacity overlying the ninth and tenth ribs in the paravertebral gutter on the left side (Figs. 1 and 2). He was admitted to hospital in March, and after bronchoscopy, when no abnormality was seen, and further postero-anterior and lateral *x*-ray films, a thoracotomy was performed by Mr. J. R. Belcher, the provisional diagnosis being a neurofibroma or ganglio-

neuroma. During the operation an encapsulated, flattened, slightly lobulated extrapleural tumour (6 by 3 cm.) was removed from the ninth and tenth intercostal spaces posteriorly. The cut surface was soft and slightly haemorrhagic, and although not quite typical the tumour was thought to be a neurofibroma.

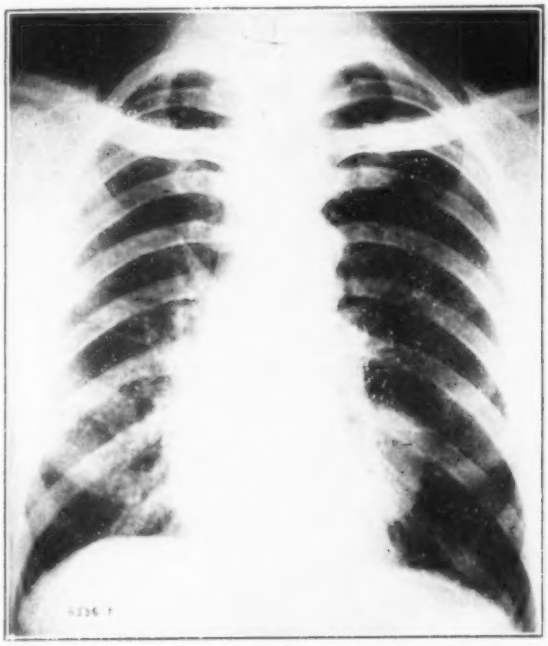

FIG. 1.—Postero-anterior *x*-ray film of chest showing a well-defined opacity (6 by 3 cm.) in the left paracardiac region overlying the ninth and tenth ribs.

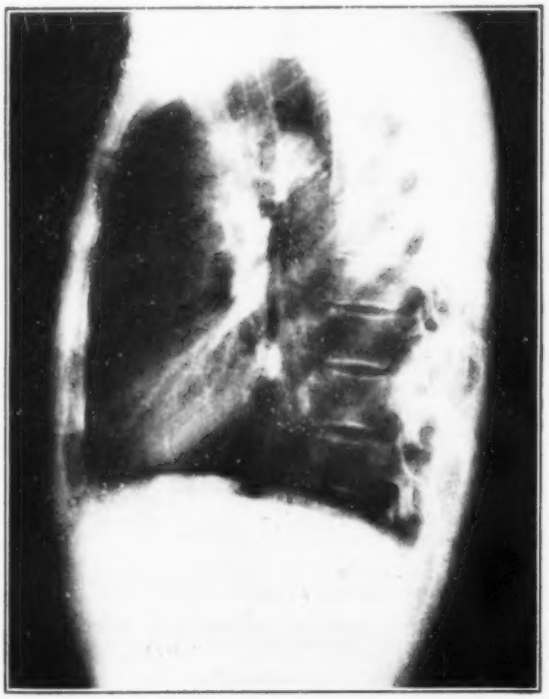

FIG. 2.—Left lateral picture showing the opacity lying in the paravertebral gutter.

Post-operatively he did not recover muscle tone and spontaneous respiration for some hours, and because of the sequence of events during recovery it was thought that he was either sensitive to D-tubocurarine or suffering from myasthenia gravis. His post-operative progress was otherwise uneventful.

The histological report on the tumour stated that "the capsule is of firm fibrous tissue but the tumour is cellular. It is made up of lymphocytes without epithelial elements."

The diagnosis is either a lymphoma or a thymoma. The position of the tumour and its encapsulation made the diagnosis of lymphoma more likely than that of a thymoma or metastasis from a malignant tumour of the thymus (Fig. 3).

In view of the histological report and his apparent sensitivity to D-tubocurarine, and after a retrospective appraisal of his history, a test dose of gallamine triethiodide was given one month after his operation. He immediately responded by complaining of diplopia, extreme lethargy, and faintness. He had difficulty in talking and swallowing and in raising his head from the pillow.

FIG. 3.—Photomicrograph of tumour showing fibrous tissue capsule and cellular tumour made up of lymphocytes without epithelial elements.

During the next few months his myasthenic symptoms became rapidly worse, although partially controlled by increasing dosage of pyridostigmine ("mestinon"). He was therefore readmitted to hospital for exploration of his anterior mediastinum with a view to thymectomy.

At operation by Mr. Belcher on September 18 the thymus was found to be enlarged, cystic, and infiltrating the ascending aorta and other structures. Total removal proved impossible. Histologically the part excised resembled the tumour removed previously.

Post-operatively he was well controlled on his pre-operative dosage of pyridostigmine until the tenth day. He then developed an urticarial rash and slight jaundice, became pale, sweaty, and dyspnoeic, with a rapid pulse, and despite additional pyridostigmine his myasthenia became rapidly worse. Although positive-pressure respiration through a tracheostomy temporarily improved his condition he collapsed and died suddenly 24 hours later. Permission for a post-mortem examination was unfortunately refused.

COMMENT

The difficulties associated with the early diagnosis of myasthenia gravis and the classification of thymic tumours are well known. In retrospect the diagnosis of myasthenia gravis in this case was plain on clinical grounds. In view of the rapidity of onset of severe symptoms the possibility of malignant thymoma with extrapleural metastasis, in a most unusual site, the paravertebral gutter, was entertained, although histologically the first tumour did not appear malignant and was not typical of a thymoma.

Normally thymomata are characterized by the presence of two types of cell—the thymocyte, a small round cell resembling a lymphocyte, and a large pale cell of reticular origin. The relative proportion of these cells varies widely from tumour to tumour, so that they may be designated lymphomas, lymphosarcomas, carcinomas, and epitheliomas (Ewing, 1940).

A search through the literature has not revealed any other case of malignant tumour of the thymus presenting as a single extrapleural metastasis.

We are indebted to Mr. J. R. Belcher and Dr. K. F. W. Hinson for their help in this case.

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POSTSCRIPT.—Since this paper was written we have seen a report by B. B. Roe (*J. thorac. Surg.*, 1957, **33**, 770) of a case of thymic neoplasm in which distinct myasthenia gravis developed six weeks after total thymectomy and radical mediastinal block dissection. The author makes two assumptions which are of interest. He suggests that all the thymic tissue was removed, although we feel that it is hard to be sure of this, and that the thymus was innocent in spite of the pathological report's suggestion that it was malignant. Moreover, expert pathological opinion indicates that any thymic tissue which is even mildly suspicious should be regarded as almost certainly malignant.

Meigs's Syndrome

That ascites and hydrothorax may be associated with an ovarian fibroma is well known, but the existence of such a syndrome is probably not so widely recognized as it should be. Thus its true incidence is difficult to estimate; Meigs (1954) in a review of the literature found 84 authentic examples. I myself have previously seen three cases (Lawson, 1950), and these are included in Meigs's figures. The case now reported illustrates how readily the condition may be mistaken for inoperable malignancy. Paracentesis abdominis was performed 50 times—far oftener than in any of the cases included in Meigs's collected series.

CASE REPORT

A (nulliparous) spinster aged 57 was referred for gynaecological opinion in February, 1956. There had been no vaginal bleeding since the menopause at the age of 40. A femoral hernia had been repaired in 1950; the medical history was otherwise negative. In September, 1953, blood appeared in the stools, and a surgeon diagnosed peritoneal carcinomatosis from cancer of the rectum. Soon afterwards ascites developed, and in December, 1953, paracentesis abdominis was performed for the first time. During the next two years this procedure was repeated at varying intervals, the abdomen being tapped altogether 48 times and a total of 470 pints (267 litres) of fluid aspirated. The fluid was always clear, and on one occasion it was examined bacteriologically with negative results. The patient complained of dyspnoea and ankle oedema as the fluid accumulated, but her general condition remained good.

By the summer of 1955 aspiration was required so often that the patient was admitted to hospital. Rectal bleeding had not occurred since the original episode, and there was no note that a pleural effusion had ever been detected. In January, 1956, another surgeon found a lower abdominal tumour and referred her for gynaecological examination.

Considering the long period of invalidism, the patient looked remarkably fit. The abdomen was grossly distended with fluid and there was a ventral hernia of moderate size. However, a firm, somewhat irregular, but freely mobile mass could be felt above the pubes. Vaginal examination was unsatisfactory. Rectal examination showed haemorrhoids, but no evidence of cancer. Clinical and radiological investigation revealed a massive right-sided pleural effusion. Systemic examination was otherwise negative. The peritoneal cavity was tapped (49th time) on February 7, and again on the 18th, the amounts of fluid being 22 pints (12.5 litres) and 23 pints (13 litres) respectively. Paracentesis thoracis was not undertaken. A tentative diagnosis of Meigs's syndrome was made, and it was decided to perform laparotomy.

At operation on February 20 a further 20 pints (11.4 litres) of fluid was aspirated; this was a dark amber colour, but contained no obvious blood. A solid, freely mobile tumour of the right ovary was noted, the pedicle of which had undergone torsion through one-quarter of a circle. The left ovary was atrophic and the uterus normal. The tumour was removed together with the right Fallopian tube. Exploration of the abdominal cavity revealed no evidence of other disease. The greater part of the omentum was removed, as it was in places adherent to the abdominal wall and presented many foramina—presumably due to the repeated paracenteses. The ventral hernial sac was excised and the abdominal wall repaired in layers. Recovery was uneventful, and a week later clinical and radiological examination of the chest showed complete resolution of the effusion. No ascitic fluid was detected after operation. At the end of a month she looked and felt fit; nothing abnormal was found in either abdomen or chest.

The tumour was a lobulated, solid mass, measuring approximately 7 by 6 by 4 in. (17.5 by 15 by 10 cm.) and weighing 4½ lb. (2,060 kg.). Although the vessels of the pedicle had been ligated, some 500 ml. of brownish fluid exuded from the tumour within 24 hours. Part of the tumour was prepared for histological examination; the remainder continued to exude fluid for several days. The cut surface presented many dilated vessels; a few appeared to be thrombosed, but there was no evidence of any gross circulatory complication. The histological appearances were those of a simple fibroma with generalized oedema and many cystic areas.

COMMENT

A detailed description of the syndrome is given in Meigs's article of 1954. Chief interest centres on the mechanisms whereby the fluid is produced and subsequently transmitted across the diaphragm. As regards the latter point, no new information has been elicited from the above case. There can be little doubt that the source of the fluid is the tumour itself. In all four personal examples the neoplasm was so moist that "waterlogged" would not be an unfair description. Two of the tumours exuded fluid amounting to about one-quarter the total weight during a period of 24 hours; in one the vessels of the pedicle were not clamped and in the other they were ligated, and it would therefore appear that most of the fluid seeps through the covering epithelium. Owing to the fibromatous nature of the tumour, it may be that the lymphatic and venous channels are obstructed, with resultant oedema. The present case illustrates that enormous quantities of fluid may be produced in a relatively short time, and one might be justified in describing the ovarian tumour as a sort of pump, collecting fluid from the circulation and diverting it into the peritoneal cavity.

Although these speculations are of much theoretical interest, the point to be emphasized is that a clinical picture closely resembling that of advanced malignancy may have a benign aetiology. The dictum of Lawson Tait (1892) bears repetition: "There is an almost universal indication for laparotomy in abdominal disease."

I am grateful to Dr. A. L. Shivas for confirming that the tumour was a benign fibroma of the ovary.

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Reviews

WATERHOUSE AND VACCINATION IN THE U.S.A.

Benjamin Waterhouse and the Introduction of Vaccination. A Reappraisal. By John B. Blake. (Pp. 95. 32s.) Philadelphia: University of Pennsylvania Press. London: Oxford University Press. 1957.

In this book, well documented, the author, who is lecturer in public health and the history of medicine at Yale University School of Medicine, sets out to show that, though Waterhouse unquestionably contributed significantly to the diffusion of vaccination in the United States, he was not a pioneer but rather a promoter. Graver still is the charge that Waterhouse for his own profit at first endeavoured to make vaccination a monopoly, and secured bonds from practitioners requiring them to remit him one-quarter of their profits in return for a supply of the virus. Waterhouse's explanation was that he restricted the use of the vaccine, which he obtained through Lettsom and Haygarth from Jenner, in order that it should not be used improperly and by "speculators in kine pock matter"; as to the bonds, they were forced on him by the practitioners he entrusted with the vaccine. On the other hand, in 1801 Waterhouse applied to Isaac Rand, the president of the Massachusetts Medical Society, for a committee of investigation into the new remedy by the society, which was ignored; and between 1799 and 1802 he furnished active vaccine to Virginia and other States through Thomas Jefferson, for which work he never asked or received any pay. He also worked hard to convince sceptics, and became one of the leading American vaccinators. Jenner regarded him as a disciple and sent him an inscribed silver box inlaid with gold. A reference to Waterhouse's professional career may be helpful in appraising him.

Benjamin Waterhouse (1754–1846) was born at Newport, Rhode Island. After a medical apprenticeship there, in 1775 he studied medicine at Edinburgh under Cullen, Black, and Monro. In 1776 and 1777 he worked with his cousin, John Fothergill, in London, eventually going to Leyden, where he graduated M.D. in 1780. Dr. Henry Viets describes Waterhouse as "probably the best educated physician who ever returned from Europe." In 1783 he was elected professor of the theory and practice of physic in the new Harvard Medical School at Cambridge, Massachusetts. Lettsom sent Waterhouse a cabinet of minerals, which enabled the American physician to introduce the science of mineralogy into the United States. Waterhouse was delicate and also had a cantankerous disposition which antagonized his colleagues at Harvard, who forced him to resign his chair in 1812. It was probably Waterhouse's egotism and airs of superiority that excited the hostility of the Boston doctors to his claims on vaccination even more than the unethical way in which he began his advocacy of the new method. Though he erred he soon repented, and is not altogether undeserving of the title of "The Jenner of America." Oliver Wendell Holmes, who had been vaccinated by Waterhouse, described him as "a brisk, dapper old gentleman, with hair tied in a ribbon behind and, I think, powdered, marching smartly about with a look of questioning sagacity and an utterance of oracular gravity."

ARTHUR S. MACNALTY.

THE ARK AND ELEPHANT STEAK

Realities of Space Travel: Selected Papers of the British Interplanetary Society. Edited by L. J. Carter, A.C.I.S. (Pp. 431; illustrated. 35s.) London: Putnam and Co., Ltd. 1957.

Mr. Carter is the secretary of the British Interplanetary Society and editor of its journal. It may be advisable to explain to medical readers that this is a scientific society with a journal which bears no resemblance to *Eagle*; and that the name of Dan Dare has been unaccountably omitted from the index of the book under review, most of which is quite incomprehensible to a reader whose higher mathematical studies were conducted in the remote past. It is concerned not with Martians with blue faces, or space helmets suggestive of juvenile delinquency, but with the dynamics of space flight, the calculation of take-off mass, aerodynamic breaking, and the determination of minimal orbits, and many of its pages consist entirely of diagrams and mathematical formulae. One gets the impression that all this is pretty good, but one turns with relief to the chapters on cosmic-ray hazards, aeromedical considerations, sensory perceptions of the weightless condition, and the problems of food on space vessels.

These chapters are almost too easy to understand, and one perhaps unjustly concludes that in the field of interplanetary flight the mathematicians are ahead of the biologists. But then they would be, wouldn't they? All the same, Dr. Shepherd on cosmic-ray hazards has a lot to say and says it very well. He explains that, though radiation hazards are unlikely to be serious for voyages just above the atmosphere, at great distances the dosage may be above the accepted level of tolerance, and that effective shielding may be too heavy. Colonel Campbell summarizes well (if occasionally ungrammatically) the better-known facts about the effects of low barometric pressures, of acceleration, and of the lack of the normal filtration qualities of air. Do you know what will happen to your otoliths on the way to the moon? As you will have to live on algae fed on human excreta you probably won't be bothered with their behaviour as a practical problem. Personally I plump for the ark and an occasional elephant steak.

RAYMOND GREENE.

STAMMERING

Stammering and its Treatment. By Franklin Brook, L.C.S.T. Foreword by Colin Edwards, M.B., B.S., M.R.C.P., D.P.M. (Pp. 134+ix. 21s.) London: Pitman Medical Publishing Co. Ltd. 1957.

In a foreword Dr. Colin Edwards states that the author of this book, as a consequence of his own stammer in his late 'teens, was led to desert the study of accountancy for that of speech therapy. Since qualifying as a speech therapist in 1947 it is evident from his observations that Mr. Brook's studies and therapeutic experiences have taken him well beyond his personal cure. The book is intended primarily for speech therapists, and in it they will find much useful information. Admittedly the treatment of stammering is still far from satisfactory, mainly because the aetiology of the condition remains obscure, but the author describes much that can be done in the attempt to overcome this speech defect by present-day therapeutic methods. Although there is nothing startlingly new as regards treatment, the various techniques are well described and practical instructions lucidly given. As the author observes, relaxation still remains an integral part of modern treatment, and a chapter is devoted to this therapeutic measure, as well as a further one on what is known as "differential relaxation," which occurs when a group of muscles is working at minimum tension and the rest of the body musculature is relaxed as much as possible.

Current views on the aetiology of stammering are reviewed, and it is not surprising to find that no final conclusion can yet be reached. It is practically certain that stammering depends on no single cause, but results from a combination of several factors which may vary in individual cases and include hereditary predisposition, developmental and environmental circumstances, and in some cases psychological abnormalities or a struggle for dominance between the cerebral hemispheres.

The treatment, in general, prescribed for adolescent and adult stammerers can be summarized as helping the patient to appreciate the nature of his stammer and the course it has followed in his particular case, and to a better understanding of himself and his relationship to other individuals. Uninhibited talking assists in promoting this

understanding, while the therapist's calm acceptance of the patient's hesitant speech will encourage the latter to give expression to his repressed feelings, and at the same time his neuromuscular tension is reduced by relaxation therapy. Various supporting methods of treatment are also described, such as voluntary stammering, repetitive or "bouncy" stammering, prolongation, the "stop and go" method, and the alteration or modification of the speech pattern. The importance of environment is rightly emphasized by the author, and there is an excellent chapter on "The Stammerer in School," from the reading of which many schoolteachers would benefit. Mr. Franklin Brook has made a valuable and up-to-date contribution to the literature of stammering, written in pleasant style and eminently readable.

C. WORSTER-DROUGHT.

PAEDIATRICS

Paediatrics for the Practitioner. Supplement, 1957. Under the General Editorship of Wilfrid Gaisford, M.D., M.Sc., F.R.C.P., and Reginald Lightwood, M.D., F.R.C.P., D.P.H. (Pp. 157+v; illustrated. Supplement alone 35s.; complete work £14 10s.) London: Butterworth and Co. (Publishers), Ltd. 1957.

The second supplement to the large work by Gaisford and Lightwood has now appeared. It is in two parts—a first section of 118 pages consisting of original articles that tell of new work in the medical and surgical paediatric fields; and a second section, called by the dreadful word "Noter-up," a 31-page cumulative supplement really, which revises and adds to the descriptions and practices of the original main volumes with which the supplement should be used.

In the first section the editors write on gamma globulins and immunity. This is a good review of the gamma globulins in health and disease and of their use in paediatrics. Gaisford writes judicially on prophylactic immunization and gives an up-to-date report on this vexed and confused subject. Paediatricians and general practitioners of much experience have used certain methods and have drawn up suggested schemes. The Departments of Health make different suggestions; and it would appear that the subject at the moment is being viewed through a poliomyelitis fog. It is to be hoped that this fog will be dispersed when immunization against this disease has become general at an early age. All the articles are good, and others include "The Use of A.C.T.H. and Cortisone"; "Tuberculosis of the Skin," by F. J. W. Miller; "Congenital Heart Disease," by John D. Keith; articles on funnel chest, neck cysts, and diseases of the genitalia by Miss Isabella Forshall; and "Galactosaemia," by G. M. Komrower. The supplement is well printed and illustrated. It is a pity that medical books are becoming so expensive.

JOHN CRAIG.

FUNCTIONAL NEURO-ANATOMY

Functional Neuro-anatomy: Including an Atlas of the Brain Stem. By A. R. Buchanan, M.D. Third edition, revised. (Pp. 362; illustrated. 56s.) London: Henry Kimpton. 1957.

This book is addressed primarily to medical students, and the author's objective is to present essential material within the minimum number of pages compatible with a proper understanding of the subject. He was successful in this with the first edition of his book and it proved popular with students, for they appreciated the functional and integrative approach to what is commonly regarded as an isolated and alarmingly complex subject.

Since 1948 a large amount of work has been done on the nervous system; many new facts have been established and many old theories have been superseded. It thus became necessary to write a thoroughly revised edition of his book, and this he has done most skilfully, for the third edition is not very much larger than the first, although it contains new material as well as 120 new, judiciously selected references. Moreover, it has not altered in character, for it still succeeds in co-ordinating the anatomy of the nervous system with its over-all functions in as logical a sequence as is possible. Despite the addition of new material, this book does not contain more than the minimum information necessary for a proper understanding of clinical neurology.

The steady increase in size of textbooks of this kind as edition follows edition is inevitable even when, as in this case, care is taken to exclude irrelevant material. Teachers cannot afford to view this trend with complacency, however, for there is an increasing tendency for medical students to be so burdened with facts that they have too little time available to co-ordinate and integrate them to the eventual benefit of clinical medicine. It is to the credit of the author of this book that he has kept this in mind in presenting the third edition of his book.

GRAHAM WEDDELL.

ABORTION

Spontaneous and Habitual Abortion. By Carl T. Javert, M.D. (Pp. 450+xiii; illustrated. 82s. 6d.) New York, Toronto, and London: The Blakiston Division, McGraw-Hill Book Company, Inc. 1957.

Dr. Javert is a practising gynaecologist with a leaning towards pathology, and has utilized his dual training in the investigation of abortion: this is defined as the termination of pregnancy before the twenty-second week, the resulting foetus weighing 500 g. (17.5 oz.) or less. The book is primarily based on a study of 2,000 specimens obtained from 2,545 abortions which occurred in the New York Lying-in Hospital during the period 1947–54, and on 471 "control" specimens obtained by therapeutic and "unintentional" abortions. The control material included 82 uteri containing an undisturbed pregnancy, a group which in itself must have offered endless scope. The whole inquiry is reckoned to have cost not less than £200,000.

With these opportunities Dr. Javert might have concentrated on the scientific aspects and dealt in detail with such matters as the anatomy of the marginal sinus, the formation and significance of the circumvallate placenta, the histology of normal and abnormal membranes, and the like. Instead he has chosen to take a wide view and to attempt the discovery of all the factors concerned in the aetiology of abortion in any one case. This, of course, is difficult, since information on such matters as undisclosed interference, the exact mode of onset of abortion, and hysterography after delivery was not available in many instances. This may explain why uterine malformation appears as an insignificant cause of abortion and why cervical incompetence is barely mentioned.

The first half of the book consists of an account of accepted modern views on normal implantation and deciduochorionic-foetal relationships, followed by a concise statement of the pathological findings in the material investigated. These, together with the references to the literature, constitute valuable information. Notable sections are concerned with abnormalities of the cord and malformations of the foetus. In the second half the author concentrates on purely clinical aspects of abortion, including its treatment. In doing so he emphasizes, possibly over-emphasizes, the psychological approach. The photographs and photomicrographs are excellent. Many of the other illustrations are cartoons (intended to be witty rather than humorous). They are delightful in themselves, but, in a book of the kind this should be, seem to me to be out of place. Having reached this conclusion, I found that Dr. Javert, in his epilogue, expected that I might do so.

T. N. A. JEFFCOATE.

The *Hospitals Year Book 1958* (Institute of Hospital Administrators, 75, Portland Place, London, W.1; 55s.) provides particulars of all hospitals in the United Kingdom, associated statutory bodies, and organizations, transfusion services, Government departments, etc. The editor's annual review of hospital services, prepared before the recent veto on the interim salary increase for administrative workers in the N.H.S., foreshadows increasing difficulties in hospital staffing due to the growing effects of inadequate pay.

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VAGOTOMY IN TREATMENT OF DUODENAL ULCER

Peptic ulcer is a common condition in Great Britain at present and causes much illness. Some idea of its incidence has been obtained in the careful survey by R. Doll, Avery Jones, and M. M. Buckatzsch[1] of the employees of a series of firms in the London area. If these findings are applied to the whole population of Britain then perhaps over a million and a half people would be estimated to have suffered or be suffering from a peptic ulcer, and about half a million to suffer from symptoms in any one year. These figures are of course only approximate, since there are likely to be geographical differences in the incidence of the disease; nevertheless they do give some idea of the size of the problem. In the sample surveyed about three out of four of the ulcers were duodenal, and these were equally prevalent in all social classes, whereas, by contrast, gastric ulcer was most frequently found in social class V and least in I and II.

Although there are indications that anxiety may play some part,[2-4] nothing precise is known either of the aetiology or of the pathogenesis of duodenal ulcer. But it is well established that patients with duodenal ulcer tend to have a more acid gastric secretion, particularly during the night, than do normal subjects, and most accepted methods of treatment have as a main aim the reduction of the level of acidity in the stomach. Treatment by medical means can produce healing of the ulcer in most cases, but unfortunately the long-term results are unsatisfactory, relapse occurring in 50–90% of patients within five years. Moreover, the ten-year mortality rate for such medically treated patients, from haemorrhage and perforation, has been found in one of the few studies of this sort to be published to be about 7%.[5] It is yet too early to say whether the new atropine-like compounds will effect any substantial improvement. What, then, has surgery to offer?

The stomach can be emptied rapidly of its contents by means of a gastro-enterostomy, but this operation results in a high proportion of anastomotic ulcers. Alternatively, secretion of acid can be diminished by the removal of part or all of the acid-bearing area of the stomach. But, until recently at least, this was associated with an undesirable mortality and an unduly high morbidity resulting directly from the effects of the operation itself. Stimulation of the vagus increases the volume and acidity of gastric secretion, and for this reason L. R. Dragstedt and F. M. Owens[6] divided the vagus nerves at the lower end of the oesophagus of two patients with duodenal ulcer; they reported encouraging results, particularly in reducing the volume and acidity of the excess overnight gastric secretion. Many surgeons adopted this procedure, but it soon became apparent that, though there was a beneficial effect on the ulcer, unpleasant side-effects were produced as a result of gastric stasis and consequent fermentation of food in the stomach. Thus the operation of vagotomy came to be combined with various other procedures such as gastro-enterostomy, pyloroplasty, or pylorectomy,[7-10] all of which enabled satisfactory emptying of the stomach to occur. This combination of vagotomy with a means of ensuring that gastric emptying is not unduly delayed produces a good result in a high proportion of cases.[7 10-12] The operative mortality is low, probably under 1%, and there is a lower incidence of dumping, of undernutrition, and of iron deficiency than occurs after the other commonly performed operation for duodenal ulcer, the Polya partial gastrectomy. The ulcer recurrence rate would unfortunately seem to be somewhat higher (about 4 to 7%), but Dradgstedt and colleagues[13] and several other investigators have shown that in such cases the vagal resection has probably been incomplete.

In an article at p. 613 of the *Journal* this week Mr. H. Burge and Dr. E. J. Pick describe the anatomical difficulties which might occur, and stress the probability that hitherto many vagotomies must have been incomplete; and in a second article (p. 615) Mr. Burge and Dr. J. R. Vane describe a method which can be used at operation to ensure complete vagal nerve section. If this turns out to be as useful in other hands as it would seem to be in theirs, the available evidence suggests that a combination of vagotomy and posterior gastro-enterostomy, or other means of preventing gastric stasis, would in most cases be a better choice than partial gastrectomy. The results are already good in about 80% of cases.

[1] Doll, R., Jones, F. Avery, and Buckatzsch, M. M., *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 276, 1951.
[2] Davies, D. T., and Wilson, A. T. M., *Lancet*, 1937, **2**, 1353.
[3] —— —— ibid., 1937, **2**, 723.
[4] Wolf, S., and Wolff, H. G., *Human Gastric Function: an Experimental Study of Man and his Stomach*, 1943, New York.
[5] Martin, L., and Lewis, N., *Lancet*, 1949, **2**, 1115.
[6] Dragstedt, L. R., and Owens, F. M., Jr., *Proc. Soc. exp. Biol. (N.Y.)*, 1943, **53**, 152.
[7] —— and Woodward, E. R., *J. Amer. med. Ass.*, 1951, **145**, 795.
[8] Crile, G., Jr., Jones, T. E., and Davis, J. B., *Ann. Surg.*, 1949, **130**, 31.
[9] Beattie, A. D., *Lancet*, 1950, **1**, 525.
[10] Edwards, L. W., and Herrington, J. L., *Ann. Surg.*, 1953, **137**, 873.
[11] Slaney, G., Bevan, P. G., and Broode, B. N., *Lancet*, 1956, **2**, 221.
[12] Lloyd Davies, J. A., *Brit. med. J.*, 1956, **2**, 1086.
[13] Dragstedt, L. R., Harper, P. V., Tovee, E. B., and Woodward, E. R., *Ann. Surg.*, 1947, **126**, 687.

and this method gives promise of ensuring a lower recurrence rate. Nevertheless, more than half the patients have had to exchange the disabilities resulting from an ulcer for those resulting from the operation (an exchange which is usually well worth while), and we must therefore look forward to the days of more effective medical control and of prevention. Until then operation should be seriously considered for any patient who has an established duodenal ulcer which is repeatedly giving rise to disabling symptoms. Which operation ? is probably not such an important question as, Which surgeon ? But any practical method of ensuring at operation that vagotomy has been complete is likely to improve the results of this operation.

OCCUPATIONAL MORTALITY

The effect of social and economic environment on mortality is a fascinating chapter of vital statistics. The early writers had little to say about occupational hazards. Galen, in his famous treatise on hygiene, said explicitly that it was not worth laying down hygienic rules for people who could not follow them and confined himself to the needs of the wealthy classes. In later centuries of the pre-statistical age the effects of occupation on health had been discussed by various writers, and by the time of Grant and Petty in the middle of the seventeenth century it was clear that the populations of the large cities were maintained only by recruitment from the country. The industrial revolution brought new hazards, and in the beginning of the nineteenth century Holland[1] showed that the cutlery trade of Sheffield, particularly dry grinding, had "a rate of mortality exceeding everything previously known in any branch of manufacture or in any pursuit or occupation." Boys who became dry grinders often failed to reach the age of 25. Little was done by way of statistical study until just over one hundred years ago, when Farr produced the first analysis of occupational mortality in the Registrar-General's Report for 1851. The twelve groups of occupations, which were well defined, were examined by ages. Farmers had the lowest death rates, and the highest rates were those of inn and beer-shop keepers, butchers, bakers, and miners. The high mortality of butchers surprised Farr, and he speculated whether an excess of meat in the diet, excess of alcohol, or the decaying matter with which they were surrounded in the slaughterhouse and its vicinity were responsible. In this period the death rate of physicians was 3.0 per 100 living and that of surgeons was 1.9, compared with 2.0 for all males aged 20 and over. Farr continued his studies, and occupational mortality became a regular decennial feature of English statistics. These earlier studies were, however, limited to samples of the population, and the occupation was not clearly defined in some cases because the industrial and occupational classifications were not identical. A man who keeps a tailor's shop or a man who sells boots may neither make clothes nor make boots ; industrially classified, these men will be tailors or shoemakers, whereas occupationally classified they are keeping a store and persuading customers to buy goods. In earlier times when a man sold the goods he made the distinction was not important, but now it is fundamental.

Continuous efforts have been made to make the classification really occupational. In 1911 the first serious attempt was made to classify all occupations by socio-economic status, and a classification by social class has been adopted in each successive census. In 1931 the mortality rates of the wives of occupied males were also tabulated for the first time in an attempt to distinguish between the occupational and environmental risk. The assumption made was that, if in any occupation the married women had a lower mortality than their husbands, then it could be fairly inferred that the excess male mortality was due to occupation and not to environment. The correlation between occupation and environment had been recognized for some time, and in 1911 the Registrar-General stated that the environmental risk should be regarded as an occupational risk if the conditions of work or the rate of pay forced a man to live in an insanitary area with an increased risk of death. The allocation of occupations to social classes presents difficulties. Some important occupations can be pursued only in a particular area: mining is bound by geographical facts ; shipbuilding to some ports ; agriculture is not an important occupation in densely populated urban areas. In spite of the difficulties and some anomalies of allocation, there is no doubt that for the main classes we do have a descending scale of socio-economic appurtenance.

This week the Registrar-General of England and Wales has issued the first *Occupational Mortality Supplement*[2] to appear for twenty years (see p. 637 for summary). It is based on the Census of 1951 and the deaths of 1949–53. One of the most striking features in this new analysis is the trend in mortality by social class. Previously the standardized mortality ratio steadily increased with descending order of social class.* For males in 1921–3 it rose from 82 for social class I to 125 for social class V ; in 1930–2

[1] Holland, G. C., *The Vital Statistics of Sheffield*, London, 1843.
[2] *Registrar-General's Decennial Supplement, England and Wales*, 1951, *Occupational Mortality*, Part 2, H.M.S.O., 1958.
* S.M.R. for males in all classes taken together is 100.

it rose from 90 to 111; but in 1949–53 the ratios for social classes I to V were 98, 86, 101, 94, and 118. The reason for this change in gradient is not clear. Of the numerically important causes of death, respiratory tuberculosis and bronchitis have a steep gradient with social class. The standardized mortality ratios of the former for classes I to V were 58, 63, 102, 95, and 143, and for the latter 34, 53, 98, 101, and 171. Members of social class I have the largest risk from vascular lesions of the central nervous system; the mortality ratios for social classes I to V are 124, 104, 101, 88, and 101. The gradient for deaths from coronary disease is even steeper: 147, 110, 105, 79, and 89. Cancer does not show a consistent trend, the ratios being 94, 86, 104, 95, and 118 for social classes I to V. It is interesting to note that the occupational group of publicans and hotel and innkeepers, to whose high mortality Farr drew attention, still have a very high death rate, the standardized mortality ratio being 150. The mortality of registered medical practitioners has improved relatively more than the mortality for all occupied males; the standardized mortality ratio in 1949–53 was 89 compared with 106 in 1930–2. The largest mortality ratios for medical practitioners were suicide 226, coronary disease 159, and vascular lesions of the central nervous system 140. The standardized mortality ratio for cancer was only 69.

As usual, infant mortality showed a gradient with social class. The rates for classes I to V were 18.7, 21.6, 28.6, 33.8, and 40.8 per thousand live births. When these death rates are split up into those related to the first four weeks of life and those related to the rest of the first twelve months, the neonatal and postneonatal death rates respectively, we find that most of the mortality is in the first four weeks. For each social class the neonatal mortality rate is higher than the postneonatal mortality rate. But the steepness of the gradient from class I to class V is chiefly due to postneonatal deaths. In other words, the main causes of death in the first four weeks do not depend so much on social class as do those in the remainder of the year.

SCHOOL HEALTH SERVICE JUBILEE

During the last quarter of the nineteenth century a growing and widening interest was taken in the health of schoolchildren both in this country and on the Continent. Children's eyesight took the first place among the earlier studies, no doubt because defects so obviously interfered with the child's capacity to profit by education—and this was the principle on which the school medical service was founded fifty years ago. The London School Board appointed Dr. W. R. Smith as a medical officer with limited functions in 1890, and three years later Bradford secured Dr. James Kerr, who was the outstanding pioneer of the service. Before the beginning of the present century the duties prescribed by the State were largely negative—such as the exclusion of children during epidemics—but in a more positive way the special education of certain groups, including the blind, deaf, epileptic, and mentally defective, was tentatively introduced. A wider view was first taken by the Royal Commission on Physical Training (Scotland) which reported in 1903. Under the influence of two great experts in health, Leslie Mackenzie and Matthew Hay, the Commission recommended in strong terms that a general and adequate system of school medical inspection should be introduced. "Such a system," they said, "is urgently demanded mainly for remedial objects, but also in order to make available information of the highest value both for ascertaining the facts of national physique and the means that may be adopted for its improvement. . . ." And they went on to say:

> "It is only by skilled medical inspection that defects in the organs of sight and hearing, or in mental development, or such physical weakness or state of nutrition as may demand special treatment in connexion with school work may be detected. We feel convinced that some of the prevailing defects in health and physique might be very materially mitigated, if not removed, by a little timely attention, and by the careful inculcation of some simple rules of health . . . which are too often completely neglected or ignored. These must be taught early if they are to become matters of habitual practice."

These wise and humane comments ring true to-day; they serve to remind us of the value of child nurture in the broad sense, and of the fact that a great deal of the remarkable improvement in the health of schoolchildren in the past half-century has been due to education—that is, the willing collaboration of teacher, doctor, and nurse.

In England a similar landmark was passed by a more circuitous route. A vague uneasiness about the physical health of recruits for the Army in the South African War was crystallized by Sir Frederick Maurice in an article published under the ominous title of "Where to Get Men." Maurice found that out of every five men wanting to enlist only two remained in the Army as effective soldiers after two years. The article gave a shock to public opinion, and it was the immediate cause of the appointment of an Interdepartmental Committee on Physical Deterioration which reported in 1904. Its original

[1] Ministry of Health. Consultative Council on Medical and Allied Services. *Interim Report on the Future Provision of Medical and Allied Services*, 1920, H.M.S.O., London.
[2] Nyswander, D., *Solving School Health Problems*, 1942, London.

terms of reference are significant: "To make a preliminary inquiry into the allegations concerning the deterioration of certain classes of the population as shown by the large percentage of rejections for physical causes of recruits for the Army. . . ." The report of this committee laid the foundations of the school medical service, which came into being in 1908. In its early days the service was chiefly confined to inspection, because its medical officers found themselves stuck in a morass of dirt and disease. Among the children in the great cities rickets and the cruder forms of tuberculosis were rife. Skin diseases caused by infestation and spread by uncleanliness prevented innumerable children from "profiting from their education," and the more serious crippling conditions could hardly be touched, because of the rush of urgent cases. Wartime conditions added to the difficulties, but at the same time they pointed the way to improvements. The inter-war period began with great advances in the care of personal health, notably in maternal and infant welfare under the 1918 Act, and in school medical work under the Education Act of 1921. Handicapped children were given more attention, and there was a strong movement to establish special schools, particularly hospital schools for orthopaedic care. At the height of the period school medical officers received constant support from the Chief Medical Officer of the Board of Education, and local authorities pressed forward with plans to promote child health. Towards the end of the 1920s a remarkable revolution took place in public cleanliness, owing partly to rising social standards, and better clothing for children and young people, and partly to a new interest in open-air activities such as bathing and games. This advance survived all the hardships of the second world war.

The present state of the school health service is conditioned by the Education Act of 1944, under which the health care of children has been extended backwards to meet the special needs of the nursery-school group and forwards to make better provision for young adolescents. Medical examination in school has now become compulsory, and the National Health Service has offered greater opportunities for both the domiciliary and hospital treatment of school-children. The services of the education authority depend as previously upon regular medical examinations carried out in the first instance by school health officers, generally employed on a full-time basis. Routine medical examination is carried out at least three times in the course of school life, and at any time a child may be examined for special reasons, either by a school medical officer or by a specialist to whom the child has been referred. There are clinics for the examination and treatment of common diseases, including those of the eyes, ears, throat and nose, and teeth; and the service makes special arrangements for the care of children suffering from mental or physical handicaps too severe for the parents to cope with unaided at home.

Where does the general practitioner come in? The answer given in the Dawson report[1] of 1920 was that school medical work should be carried out by the general practitioner at a "primary health centre," where he would be responsible for both curative and preventive aspects of child health. By now, nearly forty years after, the primary health centre has barely put in a token appearance, but under the National Health Service the general practitioner has come more into the picture, and co-operation is on the increase. The development of group practice ought still further to improve collaboration and to achieve a two-way traffic between the school health service and the general practitioner. The extension of health visiting to general practice should make the link firmer. The school medical service has not been immune from criticism on clinical grounds, and it is of great importance that an independent assessment of its work should be undertaken from time to time. During the years 1936-40 D. Nyswander[2] made a study of routine medical examinations in a district of New York. She found that routine inspections carried out by a trained teacher and school nurse, working as a team, produced rather better results, in terms of accuracy, in discovering defects than the ordinary medical inspections which were in vogue at the time. In consequence the improvements suggested were more frequent team inspections and consultations by teacher and nurse, with the duty of careful reference of any child suspected of a defect or disorder to a specially appointed paediatrician for a full examination. Recently Dr. J. A. H. Lee made a comparative study of the defects recorded at routine school medical examinations, at or near the leaving age, and the defects subsequently recorded at the medical examinations of the same men before entry to the Services. His findings were published last week (*Journal*, March 8, p. 573). Little more than half of the defects that caused rejection for the Services were mentioned in the school medical records. There was a close agreement, as one might expect, on the more "open" defects such as eyesight; but this brought into greater prominence conditions like otitis media, asthma, and cardiac lesions, in which the discrepancy was considerable.

In what direction should the school health service move during the next half-century? To begin with,

it is of the utmost importance that schoolchildren be under regular observation by those who know them at school and at home. The trained teacher and the school nurse should be able to do this, and to refer without delay any child suspected of deviation from mental or physical health to a physician for careful assessment. This physician should be a member of the service, although not necessarily on a full-time basis. He ought to know about schools to the same specialized degree as the industrial medical officer knows about the factory in which he works. If he finds a defect or disorder requiring treatment it is his duty to refer the parent to the general practitioner. If both medical and special educational care are needed, then the parent, teacher, nurse, and general practitioner must all be brought into consultation. The essential function of the school physician is to make a skilled assessment of the health of the child at school, and, after any necessary medical treatment has been given, to see that the child makes good the advantage gained.

TUBERCULOSIS IN IMMIGRANTS

There has been a good deal of controversy about the incidence of tuberculosis in people coming from other countries to live and work in Britain. Much of the discussion has been both emotional and speculative, for reasons which are understandable. At a time when the mortality from tuberculosis has fallen dramatically and when the prevalence of the disease itself seems at last to have been brought under control (some have even talked of the end of the long epidemic), it is natural to be concerned about the possibility of a fresh influx of highly susceptible or already infected subjects. There is evidence of higher susceptibility of migrants on entry into more highly industrialized communities, and evidence of high incidence of tuberculosis in some of the countries of origin of immigrants; but "no convincing evidence that the susceptibility to tuberculosis or the course of tuberculosis is dependent on the degree of pigmentation of the skin or any other racial factor."[1]

Facts have been scanty or sometimes obtained from small and biased samples incapable of supporting trustworthy generalizations. But two investigations throw light on the problem. In 1954 a survey was made of five major hospital units in the North-west Metropolitan Hospital Region.[2] It suggested that the number of Irish-born tuberculous patients was three times higher than the number expected by comparison with the tuberculous patients born in the Greater London area. E. V. Hess and N. Macdonald concluded that this higher prevalence of disease in Irish immigrants was less due to the recrudescence of existing lesions than to the fact that a large proportion were of rural stock, non-reactors to tuberculin, and within the susceptible young adult age group. They were therefore immunologically ill-equipped to meet the high risks of infection in the urban centres in which they sought employment. These authors suggested that B.C.G. vaccination before leaving Ireland and a follow-up scheme in Britain should be considered. Now G. Z. Brett[3] has analysed the 32,000 examinees attending a static mass radiography centre during 1956 according to place of birth and date of arrival. The incidence of active cases of pulmonary tuberculosis (those needing treatment or close supervision) was compared for four main groups of immigrants (Irish, Cypriot, West Indian, and a residue of heterogeneous birthplace) and a control group of examinees born in the United Kingdom. Taking age, occupation, and sampling errors into account, the author finds an excess incidence in Irish immigrants at least three and probably nearer seven times that in the control group. An excess incidence was also found in Cypriots, but not in West Indians. An important difference from the earlier study was the absence for Irish immigrants of any rising gradient of incidence of pulmonary tuberculosis with length of stay. The excess incidence appeared to operate from the time of entry; "active tuberculosis in Irish immigrants was either present at higher than normal rates on arrival in England or developed soon after as a result of new, or the breakdown of an already existing, infection."

These facts enable a sense of proportion to be kept. The more serious problem is not the new factor of West Indian immigration but the older and more familiar factor of the Irish influx. But there is still a problem which ought not to be evaded, in the interests of migrants and hosts alike; in 1954, for instance, no less than 10% of cases on the Irish registers had returned from England with the disease. Medical examination of West Indians has been resisted on the grounds that they are British subjects and ought not to be subjected to more interference than are other groups of British subjects (though U.K.-born migrants to Commonwealth countries are required to undergo chest radiography). The same objection cannot be raised to *x*-raying Irish immigrants. B.C.G. vaccination is offered in Ireland (and in Cyprus), but it is not proceeding fast enough to achieve universal protection, and there is justification for giving some priority to migrants. Equally, so far as existing, and unsuspected, disease is concerned, intending migrants should not complain if the case-finding machinery is more intensively directed towards them. The need for some action springs from the simple fact that tuberculosis is a preventable disease.

LABORATORY SERVICES IN SCOTLAND

When the National Health Service came into being in Scotland the existing laboratories were of two distinct types: on the one hand were the dominant university departments, and on the other the usually inadequate and sometimes non-existent laboratory facilities in hospitals outside the four teaching centres. Great strides

[1] Holm, J., *Transactions of Fourth Commonwealth Health and Tuberculosis Conference, London, 1955*, 1956, London.
[2] Hess, E. V., and Macdonald, N., *Lancet*, 1954, **2**, 132.
[3] Brett, G. Z., *Tubercle* (*Lond.*), 1958, **39**, 24.

have been made since 1948, and the cost of the laboratories has mounted almost twice as fast as has hospital expenditure generally. But, despite the fact that many areas of dense population now have laboratory services that would have seemed a pipe-dream ten years ago, these have proved to be seriously inadequate in the face of increasing commitments, caused primarily by the upgrading of many of the peripheral and even of some central hospitals. Thus it is that those responsible for the day-to-day working of these laboratories feel that their clamant demands for expansion have been neglected or ignored, sometimes in favour of the less pressing needs of the teaching hospitals, which, they claim, are favoured by closer contacts with their regional boards. It is probable that the different administrative structure in Scotland has contributed to the difficulties; the five regions are geographical; the boards of management have none of the executive powers invested in the boards of governors of the English teaching hospitals; and there is no independent public health laboratory service.

In April, 1956, the Scottish Health Services Council appointed a committee to examine afresh the whole problem of the organization of the laboratory services. Its report has now been published.[1] No centralization of laboratory services is proposed, nor is the creation of a public health laboratory service as in England and Wales. The hospital laboratories are therefore committed to provide an integrated service for general practitioners, local authorities, and hospital patients. Significantly the report states, "Laboratories should be located at hospitals." Again, while no basic alteration in administrative structure is advised, changes of the first importance are recommended to unify and strengthen the advisory machinery. The present arrangements are haphazard; they vary in pattern and in effectiveness from region to region and are much at the mercy of the interest, or lack of it, of the individual board of management. The committee's recommendations elaborate and amplify the system which has evolved in the Western Region, based on Glasgow. The report proposes the appointment by regional boards of a Regional Advisory Committee on Laboratory Services, consisting of members of the regional board, laboratory consultants, general practitioners, and medical officers of health, together with hospital consultants other than those engaged in laboratory medicine. The laboratory consultants would be representative of the peripheral and non-teaching as well as of the teaching hospitals, and they would be in a minority on all the committees. At national level a similar committee would replace the existing Joint Committee on Laboratory Services, which has never properly fulfilled its intended functions. This new committee would provide the necessary liaison with the regional committees through common membership, and would have the right to tender advice directly to the Secretary of State. The important feature is that continuity of representation of all the different interests would be assured—from local sectors through the Regional Advisory Committee to the National Standing Advisory Committee and so to the Secretary of State. These are the main proposals. Others of detail are equally well considered and meet most of the points raised by those who gave evidence to the Committee on Laboratory Services in Scotland on behalf of the Scottish Council of the B.M.A. It is sincerely to be hoped that this careful study with its thoroughly practical recommendations will be implemented. If so, it will be a stimulating influence to the progress of laboratory medicine in the whole of Scotland, and the scheme proposed may well prove worthy of adoption in other parts of the United Kingdom.

[1] Department of Health for Scotland—Scottish Health Services Council. *The Organization of Laboratory Services*. 1958. H.M.S.O., Edinburgh. Price 1s. net.

HISTORY OF MEDICINE

The History of Medicine Section of the Royal Society of Medicine was founded on November 20, 1912. William Osler was elected the first president, for it was his quickening and magnetic influence that brought it into existence. Raymond Crawfurd and D'Arcy Power were chosen as secretaries, and among the list of vice-presidents and members of the council were the names of Allbutt, Ronald Ross, H. D. Rolleston, E. Muirhead Little, J. A. Nixon, and F. M. Sandwith. The section has continued for over 40 years to promote the historical study of medicine by the high standard of its communications and the distinction of the presidents and members of its council. It has fulfilled Osler's hope that it would form a meeting-ground for scholars, students of the subject, and all who felt that the study of the history of medicine had a value in education.

In commemoration of the jubilee of the Royal Society of Medicine the council of the society decided to publish in book form a selection of papers which had been presented to the History of Medicine Section during the past 40 years. Entitled *Sidelights on the History of Medicine*,[1] the book has been edited by Sir Zachary Cope, a past president of the section. The wealth of material made the choice difficult, but the selection has been ably done. In its 23 chapters by dead and living medical historians the book ranges from Ancient Egypt and the origins of anatomical science, by A. J. E. Cave, to Wilhelm Conrad Röntgen (1845–1923) and the early development of radiology, by E. Ashworth Underwood. It may also be mentioned that Charles Singer writes on medical science in the Dark Ages, A. P. Cawadias on the Royal College of Physicians and its bombing in the second world war, K. J. Franklin on the work of Richard Lower (1631–1691), Sir Zachary Cope on surgical lectures of 150 years ago, and Douglas J. Guthrie on the patient—an important but neglected factor in the history of medicine. The other articles are equally readable and interesting. No paper by Osler is included, for his contributions to the section were few, but the whole book is a tribute to his memory as founder, and evidence that the seed he sowed has borne fruit.

[1] *Sidelights on the History of Medicine*. Edited by Sir Zachary Cope. (Pp. 246+x; illustrated. 45s. 35s. to Fellows of the Royal Society of Medicine.) London: Butterworth and Co. (Publishers) Ltd. 1957.

OCCUPATIONAL MORTALITY

NEW DATA FOR ENGLAND AND WALES

Mortality by occupation and social class for England and Wales in the years 1949–53 is analysed in the Registrar-General's Decennial Supplement issued this week.* Many differences are recorded from the data provided by the previous analysis, which was published twenty years ago and related to the years 1930–2.

Social Class Variations

A striking change is the mortality by social class, in that for the first time, as Table I shows, the mortality of adults does not rise in a steady gradient from class I to class V.

TABLE I.—*Mortality by Social Class, England and Wales*

	Males S.M.R. 20–64			Married Women S.M.R. 20–64		Single Women S.M.R. 20–64	
	1921–3*	1930–2	1949–53	1930–2	1949–53	1930–2	1949–53
All occupied and retired ..	100	100	100	100	100	92	85
Social class I	82	90	98	81	96	100	82
,, ,, II	94	94	86	89	88	64	73
,, ,, III	95	97	101	99	101	95	89
,, ,, IV	101	102	94	103	104	102	89
,, ,, V	125	111	118	113	110	112	92
Unoccupied ..	—	135	124	134	95	122	142

* Excluding non-civilians.

The standardized mortality ratio (S.M.R.) refers to adults aged 20–64 inclusive. For any particular category of adults it is obtained by dividing the number of deaths in that category during 1949–53 by an expected number of deaths and multiplying by 100. The expected number of deaths is the number that would have occurred if the death rates in each age group in the category had been the same as in a standard population in England and Wales. *Thus the S.M.R. of 98 for social class I males means that their mortality was 98% of the mortality for all males in the same age group (20–64) in England and Wales.*

Class I includes professional occupations, such as medicine, law, the Church; class II managerial occupations, such as employers, managers, farmers; class III skilled occupations, such as fitters, clerks, engine drivers; class IV semi-skilled occupations, such as machine minders; class V unskilled occupations, such as labourers, kitchen hands. Social class and occupation of married women are derived from those of their husbands.

Changes in the composition of social class IV may largely explain the relative improvement of mortality for men in that class, but they are not sufficient to explain the improvement of class II in relation to class I.

For some causes of death the mortality rate usually rises in a gradient from social class I to V. For other causes of death the gradient tends to fall, while for some causes of death a different relationship is shown to social class. Some of the main causes of death classified thus are as follows:

Mortality Rises from Class I to V.—Tuberculosis, carcinoma of stomach, carcinoma of lung (men only), chronic rheumatic heart disease, bronchitis, pneumonia, peptic ulcer.

Mortality Falls from Social Class I to V.—Acute poliomyelitis, leukaemia, carcinoma of lung (women only), coronary diseases (men only), carcinoma of breast (women only), hyperplasia of prostate.

Mortality Differently Related to Social Class.—Diabetes mortality of males falls from class I to IV, then rises. Accidental death in the home is high in I and V. Psychosis as a cause of death is high in I and V. No relationship between mortality and social class has been detected for nephritis and nephrosis in males, or for vascular lesions of nervous system, coronary disease, and duodenal ulcer in women.

Geographical Variations

In general, mortality is higher in northern and north-western England and in Wales than in southern and south-eastern England. This remains true when adjustments are made for variations in the proportions of the social classes in the different parts of England and Wales.

With an S.M.R. of 100 for England and Wales may be compared the following S.M.R.s for men:—North-western region: class I, 101; class II, 103; class III, 114; class IV, 107; class V, 137. Southern region: class I, 97; class II, 80; class III, 87; class IV, 81; class V, 89. Wales: class I, 103; class II, 95; class III, 123; class IV, 101; class V, 121.

Of the conurbations Greater London is for men the most healthy, and Merseyside the least. The S.M.R. for social class I in Greater London is 94, and for class V, 113. The corresponding figures for Merseyside are 101 and 149.

For married women Greater London is also the most healthy conurbation, but Tyneside is the least. In Greater London the S.M.R. for married women in social class I is 105, and in class V, 91. Corresponding figures for Tyneside are 100 and 145.

The rural districts have much lower mortality rates than any of the conurbations. For men they are as follows: social class, I, 105; II, 74; III, 87; IV, 77; V, 93.

Deaths from respiratory diseases show a very steep gradient by social class, and particularly so in urban areas. In the conurbations as a whole the S.M.R.s for men are as follows; class I, 62; II, 74; III, 115; IV, 127; V, 172. The figures for married women are class I, 73; II, 66; III, 110; IV, 135; V, 156.

Medical Practitioners

At the 1951 census 34,120 medical practitioners in the age group 20–64 were enumerated. During 1949–53, 1,008 of them died instead of 1,129 as would have been expected from the male mortality rates for the country. This gave an S.M.R. of 89, which was a considerable improvement on the S.M.R. of 106 for 1930–2.

With the S.M.R. for all men aged 20–64 in England and Wales being 100, the doctors had an S.M.R. due to poliomyelitis of 800—that is, 8 times as many deaths as expected from that disease. Deaths of doctors from some other diseases showing particularly high death rates in the medical profession gave S.M.R.s as follows, each S.M.R. being comparable to 100 for all men of 20–64 in England and Wales for the diseases shown: diabetes 140, psychoses 200, general arteriosclerosis 200, nephritis and nephrosis 120, cirrhosis of liver 240, cholelithiasis and cholecystitis 250, suicide 226, vascular lesions of nervous system 140, and coronary disease 159.

While 8 deaths in this group of medical practitioners were assigned to poliomyelitis instead of 1 expected, the report points out that members of the legal profession had 7 deaths from this cause instead of only 1 expected. Ten deaths of medical practitioners were assigned to leukaemia

TABLE II.—*Numbers of Deaths Due to Cardiovascular Disease Registered and "Expected" and S.M.R.s for Members of Medical, Clerical, and Legal Professions, England and Wales, 1949–53*

Cause of Death	Medical Practitioners			Ministers of Religion			Judges, Barristers, Solicitors		
	Regd.*	Expd.†	S.M.R.	Regd.	Expd.	S.M.R.	Regd.	Expd.	S.M.R.
Coronary thrombosis, angina ..	287	180	159	308	203	152	123	102	121
Vascular lesions of nervous system ..	106	76	140	118	88	134	52	44	118
Hypertension	37	32	*116*	39	36	*108*	25	18	139
Chronic endocarditis not specified as rheumatic	2	9	(*22*)	3	9	(*33*)	5	5	(*100*)
Other myocardial degeneration ..	21	37	57	33	44	75	14	21	67
General arteriosclerosis ..	10	5	*200*	4	7	(*57*)	4	3	(*133*)
Total ..	463	339	137	505	387	130	223	193	116

* Registered deaths. † "Expected" deaths. S.M.R.s in italics are based on 10–49 deaths, those in italics and parentheses on fewer than 10 deaths.

**Registrar-General's Decennial Supplement, England and Wales, 1951, Occupational Mortality*, Part 2, 1958. H.M.S.O. (7 guineas for 2 vols.).

instead of 7 expected in the age group 20–64. This is not a significant excess, but there were a further 9 deaths from this cause among doctors aged 65 and over which gave them a mortality 225% of the average. There was a tendency for the suicide rate to fall with increasing age. This was not present to the same degree among members of social class I generally. Mortality from tuberculosis was low, and lower than among class I as a whole. Only 18 deaths were assigned to bronchitis instead of 76 expected, giving an S.M.R. of 24. Table II shows the S.M.R.s for medical practitioners, ministers of religion, and lawyers for cardiovascular diseases.

Mortality from heart disease is similar among medical practitioners and ministers of religion, and higher in both those professions than in the legal profession. The low death rate from myocardial degeneration in all three groups is thought to reflect the low mortality from bronchitis among the professions.

Some Occupational Groups

Occupational groups with high death rates included the following (with S.M.R.s for all causes of death in parentheses): slate masons (467), tunnel miners (225), getters in mines, not coal (222), glass blowers (189), drivers of horse-drawn vehicles (189), haulage contractors (175), sand blasters (173), furnace men (154), hewers and getters in coal mines (153), land agents (150), publicans and hotel owners (150), leather dressers (149).

Occupational groups with high death rates from coronary disease include bus and tramway managers (221), land agents (214), haulage contractors (204), Roman Catholic priests and monks (193), pharmacists (193), and tailors (184).

Glass blowers have a high S.M.R. (350) for bronchitis, for "other myocardial degeneration" (300), vascular lesions of nervous system (200), and cancer of lung (200). Sand blasters also have very high S.M.R.s on the average—for instance, suicide (300), pneumonia (300), cancer of lung (250), cancer of stomach (200), respiratory tuberculosis (450).

Workers underground in coal mines have exceptionally high mortality ratios for cancer of stomach, and exceptionally low ratios for cancer of lung. Pneumonia is exceptionally prevalent as a cause of death among workers in iron foundries and furnace-men.

High S.M.R.s for suicide are found in the following occupations (in addition to medicine): farmers (200), gardeners and nurserymen (149), other agricultural workers (166), owners of hotels and inns (175). Exceptionally low ratios are recorded for drivers of stationary engines (50), constructional engineers (46), platers (44), radio mechanics (40), makers of alcoholic drinks (37), steel foundry labourers (37), paint sprayers (20), Roman Catholic priests and monks (19). All these low S.M.R.s are derived from small numbers of deaths, and consequently are rather unreliable.

Infant Mortality

The infant mortality rate increases by social class from I to V, but the steepness of the gradient is mainly in the deaths after the first four weeks of life. Table III shows this.

Infant mortality rates show considerable differences within the social classes. While the rate for class II as a whole is 21.6 deaths of legitimate infants per thousand live births, the rate for babies born to fathers engaged in entertainment and sport is 23.5 and for fathers engaged in personal service is 27.8. The rate for social class III as a whole is 28.6, but for babies born to fathers in mining and quarrying occupations it is 45.5. For class IV as a whole the rate is 33.8, but for babies born to fishermen it is 55.1.

Stillbirth rates increase by social class as follows, the figures being the stillbirth rate per thousand total births: class I, 16.3; II, 19.9; III, 22.5; IV, 24.5; V, 27.4. The rates for illegitimate stillbirths are about 50% higher and show a similar gradient, except that the rate for class I, which is based on small numbers, is unusually high.

TABLE III.—*Infant Mortality Rates by Social Class, England and Wales*, 1949–53

	All Classes	Social Class				
		I	II	III	IV	V
Infant mortality	29·5	18·7	21·6	28·6	33·8	40·8
Neonatal mortality	18·6	14·0	15·6	18·3	20·0	22·8
Postneonatal mortality	11·0	4·7	6·0	10·4	13·7	18·0

Reports of Societies

CONTROL OF HELMINTHIASIS

Recent work on the control and treatment of helminthiasis was the subject at a meeting of the Section of Comparative Medicine of the Royal Society of Medicine on February 19.

Immunization of Cattle

Dr. W. F. H. JARRETT (Veterinary Hospital, Glasgow), speaking of work done by himself and his colleagues (Drs. W. I. M. McIntyre, W. Mulligan, F. Jennings, and G. M. Urquhart), said that there were three possible means of controlling helminth infestation: by effective measures of general hygiene, by anthelmintic treatment, and, least studied of all, by the production of active immunity. Lung-worm disease (husk) in cattle and sheep was a serious cause of economic loss and death of animals in parts of Britain. It affected young animals most severely. The developing larvae migrated to the lungs, where they caused pneumonia. A complement-fixation test with an antigen prepared from adult worms had been used to assess the antibody response in naturally infected animals. A rise of titre occurred about 45 days after primary infection, but subsequent challenge of the animal would result in a subsidiary rise in antibody titre after only about 7 days. Antibodies were found in the gamma-globulin fraction of the serum proteins, and in calves passive immunity could be produced by injecting gamma globulin.

Attempts to cause active immunity had led to study of methods of attenuation of living larvae. It had been found that *x*-irradiation resulted in attenuation of the larvae: they could then be kept alive for at least 20 weeks in the laboratory but were rapidly destroyed after oral administration to non-immune animals. Their destruction appeared to take place mainly in the mesenteric lymph nodes, and very few such irradiated larvae succeeded in passing beyond this barrier to reach the lungs and become mature. Nevertheless, effective antibody titres were found in the animal's serum, and subsequent challenge of the immunized animal showed that a high degree of resistance had been produced. Field trials by oral administration to calves of 1,000 irradiated larvae had been carried out and had shown highly significant protection. Studies were continuing on the duration of the active immunity, and also on other methods of attenuating the larvae. Radioactive cobalt (gamma-ray irradiation) had been found to have a similar effect to *x*-irradiation. Dr. Jarrett emphasized how the cost of animal trials of this kind was a limiting factor in the work.

Experimental Chemotherapy

Dr. J. K. WALLEY (I.C.I., Macclesfield) spoke about the removal of lung-worms in domestic animals. He stressed the difficulty of screening various chemical compounds for anthelmintic action, because the worms tended to be host-specific. It was therefore necessary to attempt to cause these helminths to parasitize the small laboratory animals. It was now possible to cause the three main species of lung-worms to infect guinea-pigs. Cyanacethydrazide had been found effective in expelling adult lung-worms, though it did not affect migrating larvae. A means of assessing the efficacy of the compound in calves and similar animals consisted in making a fistulous opening into the trachea and inserting a tube to the outer opening of which a

polythene bag was attached. The bag was replaced daily, and the content of exudate and worms could be measured. Thus the efficacy of a compound in causing expulsion of worms from the air passages could be assessed.

Dr. O. D. STANDEN (Wellcome Laboratories of Tropical Medicine, London) spoke on the experimental approach to chemotherapy in helminthic diseases. This could be either selective or empiric. In the selective approach a known effective compound was analysed and its related compounds studied to see if modifications of their chemical structure might result in an effective compound free from some of the disadvantages of the original substance. Since only a few effective anthelmintic compounds were known, the selective approach was not very fruitful. The empiric approach depended upon screening a very large number of compounds in the hope that one or more might be found with some anthelmintic action. From that discovery the selective method might then be applied. In the field of schistosomicides, Dr. Standen mentioned lucanthone hydrochloride as an example of a substance discovered empirically, subsequent study of whose related chemical compounds had as yet added no new effective substance. The selective approach based on the known properties of trivalent antimony compounds had resulted in other schistosomicidal drugs with less toxic effects and suited to intramuscular administration, but with lower activity. The development of trivalent sodium antimony gluconate was an advance in that fewer injections were required.

In screening various compounds it was necessary to use laboratory animals. In these the parasites of humans might mature, or else a related parasite to the one of humans might be available. Sometimes it might be necessary to test a compound against several animal parasites in order to assess its action against a parasite in man. The site in which the parasite lodged in man and in test animals must be considered in assessing the action of anthelmintics. *In vitro* testing of compounds was much less satisfactory because drugs were often modified by absorption and metabolism in the body, and because the site of the parasite in the animal body could not be imitated.

In conclusion, Dr. Standen referred to the development of piperazine compounds effective in human oxyuriasis and ascariasis which had first been tested against the threadworm of the mouse (*Aspiculuris*). Recently certain quaternary ammonium compounds had been discovered to have an action against a worm (*Nippostrongylus*) in the rat, and it was possible that these might prove effective in strongyloidiasis and hookworm in humans and in parasitic gastro-enteritis in sheep and cattle.

Preparations and Appliances

USE OF POLYVINYL FEEDING-TUBE

Dr. J. J. KEMPTON, paediatrician, Reading, and JEAN M. MURRAY, S.R.N., S.C.M., R.S.C.N., sister-in-charge, premature baby unit, Reading, write: The use of the indwelling plastic feeding-tube as described by Royce and others (1951) is an important advance in the care of premature, damaged, or sick newborn infants; it has been adopted in a number of centres, but the technique deserves to be more widely known.

We have used polyvinyl tubes in a series of 100 premature infants. They have also been used in some full-term babies suffering from cerebral damage or from congenital heart disease with cardiac failure. The apparatus (Fig. 1) is an extremely flexible tube, 21 in. (53 cm.) long and 1 mm. internal diameter, and has a catheter end with two lateral holes. It is sterilized by boiling, and passed into the infant's nose to a point marked by a thread which is at ½ in. (1.3 cm.) more than the distance from the bridge of the nose to the xiphisternum. A very small amount of the first feed of glucose-saline is then slowly injected by syringe. Any resistance may mean kinking of the tube, which may need to be withdrawn a little and reinserted. There is a characteristic "feel" of absent resistance when the tube is in the stomach, and injection of the first few drops of clear fluid produces no reaction in the baby.

The tube is then fixed, and subsequent feeds are given by funnel, the cot-head being tilted up during, and for half an hour after, the feed. Two spigots are used and are changed at each feed, the one not in use being kept in

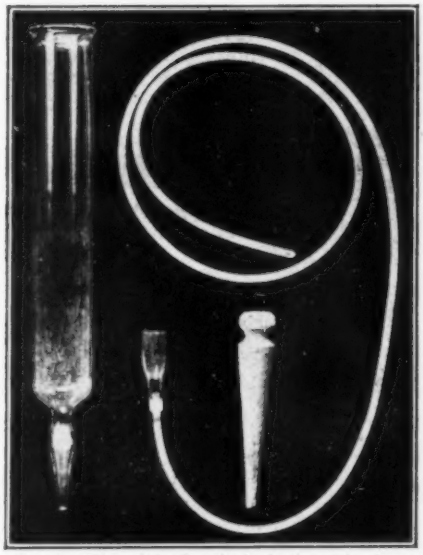

FIG. 1.—Glass funnel, polyvinyl tube and spigot.

Milton solution. The tube is kept in for four to five days, and if properly fixed (Fig. 2) is not dislodged by the baby's movements. It is removed by cutting the adhesive strapping, which is then left to separate gradually, as stripping off may damage the skin.

Feeding by this method is replaced by ordinary tube-feeding with a rubber catheter in small premature babies; in larger ones or full-time infants breast- or bottle-feeding can be gradually introduced while keeping the tube in position.

Cyanotic attacks associated with feeding procedures are almost completely eliminated by this method, and more frequent feeds and a greater total amount can be given. The insertion of the tube is a skilled paediatric nursing procedure, but subsequent feeds, through which the baby often sleeps, can be safely left to a student nurse, or nursery nurse, after instruction.

FIG. 2

Of the 100 premature babies fed initially in this manner, 95 survived. One died on the third day of pneumonia, two had kernicterus of prematurity, and two had multiple congenital abnormalities. The remaining 95, whose average birth weight was 3 lb. 13 oz. (1,730 g.), regained their birth weight in an average period of 14 days.

A little mucoid nasal discharge occurred in seven cases, but there was no significant nasal infection. Even so, it seems that this might occur, and that this is a method of feeding for use only in premature and neonatal units in which measures for preventing the spread of infection are kept at a really efficient level.

The polyvinyl tubes are obtainable from Portland Plastics, Ltd., Basset House, Hythe, Kent, and the glass funnels from Albert Brown Ltd., Chancery Street, Leicester.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Porphyria

SIR,—Numerous attempts have been made during recent years to provide a satisfactory classification of the porphyrias. All workers are agreed that congenital porphyria (Günther) is a distinct clinical and pathological entity in which abnormality resides in the haemopoietic system. The acute porphyria and porphyria cutanea tarda of Waldenström[1] appear to involve the liver rather than the haemopoietic system and were therefore grouped under the heading "hepatic porphyria" by Watson *et al.*,[2] to distinguish them from the "haemopoietic" congenital porphyria. Schmid, Schwartz, and Watson[3] later recognized a mixed porphyria of hepatic type to accommodate cases in which symptoms were present resembling those of both acute intermittent porphyria and porphyria cutanea tarda.

My own investigations led me[4] from 1952 to emphasize the biochemical differences between those patients exhibiting abdominal colic, large output of urinary porphobilinogen, not infrequently nervous symptoms but without photosensitivity or other lesions of the skin (acute intermittent porphyria) from patients on whom lesions of the skin were present. These latter excreted little if any urinary porphobilinogen but large quantities of faecal porphyrins; they seemed to be best accommodated under porphyria cutanea tarda, and familial incidence could frequently be demonstrated (see Holti, Rimington, Tate, and Thomas[5]). At the same time, evidence was steadily accumulating that a condition very similar to porphyria cutanea tarda could arise as a result of chronic alcoholism[6 7] or malnutrition associated possibly with other hepatoxic factors.[8 9] Convincing proof of the possibility of symptomatic cutaneous porphyria was afforded by the case of a woman with a porphyrin-producing liver-cell adenoma.[10 11] The classification of the hepatic porphyrias required revision, and this has been admirably accomplished, to my mind, by Waldenström,[12] who proposes the following:

(1) Porphyria cutanea tarda symptomatica:
  (i) Alcoholic cirrhosis
  (ii) Bantu cirrhosis
  (iii) Exceptional cases
(2) Porphyria cutanea tarda hereditaria:
  Protocoproporphyria
(3) Acute intermittent porphyria.

In their recent publication Drs. Geoffrey Dean and H. D. Barnes (*Journal*, February 8, p. 298), however, discard acute intermittent porphyria and propose to recognize the "Swedish type of porphyria hepatica" and the "South African type." The latter differs essentially from the former in just those features which I have already insisted serve to distinguish porphyria cutanea tarda from acute intermittent porphyria—namely, in the presence of skin lesions, a continued large production of porphyrins which are eliminated mainly in the stool (even during clinical remission), and absence of porphobilinogen from the urine or its excretion in only relatively small amount during acute exacerbations of the disease. Until the precise biochemical error has been revealed which is in each case responsible for the manifestations of disease in porphyria patients, a truly satisfactory classification cannot be drawn up. I submit, however, that in our present state of knowledge the classification of choice is that due to Waldenström.[12]—I am, etc.,

London, W.C.1. C. RIMINGTON.

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Indicators of Irradiation Damage

SIR,—I was interested to read Surgeon Commander P. W. Edmondson's paper (*Journal*, February 15, p. 363) on the effects of chronic gamma irradiation in female guinea-pigs and also the annotation (p. 391) on indicators of chronic irradiation. A preliminary report has been published[1] on quantitative examinations of bone marrow in young male guinea-pigs after acute whole-body gamma irradiation using a cobalt-60 unit as source. Subsequent experiments have confirmed the findings in this report. In the same experiments estimations of blood leucocyte levels were also made at various periods after irradiation.

Quantitative analysis of the immature neutrophils in the marrow shows a steady decline from the fourth hour after irradiation until the fourth day. After an initial and transient polymorphonuclear leucocytosis occurring at the fourth hour, the blood neutrophil level remains within normal limits until about the fourth day, when a decline commences. A partial recovery of the immature neutrophils in the marrow occurs from the fourth to the eighth day and this is followed, after an interval of four days, by the well-known "abortive rise"[2] in blood neutrophils which occurs from the eighth until the twelfth day. A second decline, which is both marked and progressive, occurs in the marrow levels of immature neutrophils after the eighth day, and this is reflected four days later—i.e., from the twelfth day—by a precipitous fall in blood neutrophils. There is the same lag period of four days in the recovery phase. The immature cells show a marked increase after the sixteenth day, but blood neutrophil levels do not show a definite increase until after the twentieth day. Thus at all times there is a lag period of four days between changes in the marrow population of immature neutrophils and the blood population of mature neutrophils.

Recovery of erythropoiesis in the marrow, as shown by increasing numbers of erythroblasts, occurs from the tenth day after irradiation and is followed, after four days, by a rise in blood reticulocytes and the presence of substantial numbers of polychromatic and orthochromatic erythroblasts in the peripheral blood. The increase in marrow erythroblasts, which is particularly rapid and marked between the fourteenth and sixteenth days, is quickly reflected in the peripheral blood (within two days) by the presence of large numbers of polychromatic and orthochromatic erythroblasts and also reticulocytes.

A correlation can be made between blood and bone marrow cellular levels, especially if the marrow cells are estimated by a quantitative technique rather than by a percentage count. The fallacy of estimating blood leucocyte levels solely by percentage count is widely recognized by clinicians, and the same reasoning should be applied to estimations of bone-marrow populations. Unfortunately, in the human, quantitative estimations of marrow cells tend to be rather variable owing to the varying dilution of marrow aspirate by blood.

One realizes, of course, that the effects of chronic irradiation on the haemopoietic organs differ from those after acute irradiation. However, the effects of the latter are of significance in the event of atomic warfare or after accidents involving peaceful uses of radioactive materials. Thus a knowledge of the time lapse, in man, between changes in marrow and blood granulocyte levels might be of some application, firstly, in assessing cases where exposure to severe acute irradiation had occurred but dosage was indefinite, and, secondly, in assessing the response to myelotherapeutic measures such as bone-marrow transfusion.—I am, etc.,

Bristol, 8. P. F. HARRIS.

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"Diminished Responsibility" Manslaughter

SIR,—Your legal correspondent (*Journal*, March 1, p. 527) records a life sentence for a "diminished responsibility" manslaughter. He states "there is not much difference for Bastian in having been found guilty of manslaughter instead of guilty of murder but insane."

The only similarity is that the offender is subject to an indeterminate period of detention. The difference, and a critical one, is that in the one case the offender is committed to prison as a convicted felon, with no guarantee of treatment directed to the cause of his diminished responsibility; in the other case he becomes a Broadmoor patient and is committed to an institution specifically devoted to the care and treatment of persons of unsound mind.—I am, etc.,

Crowthorne, Berks. PATRICK G. MCGRATH.

Disease Education by the B.B.C.

SIR,—Man has aye been entertained by the sufferings of his fellow men. For the Romans it was the agony of the dying gladiator that gladdened the heart; we content ourselves with the drenching of the clown, or savour suffering in imagination only as in the novel. But it grieves me that a leader of our profession should, in his public demonstration of his patient suffering from heart failure, lend himself to this beguilement. For let those sincere men, striving to help suffering humanity by a process of education, know that this was the end of their toils—a common spectacle, a vulgar entertainment.

Let them know also that they are rendering harder the task of those of us who, in this age of scientific materialism, are striving by precept and example to imbue our students with the humanity of our profession.—I am, etc.,

Cramlington, Northumberland. GEORGE DAVISON.

SIR,—Since I have seen only one of the television series *Your Life in Their Hands*, it would be wrong for me to comment on the others. In this letter I do not even wish to discuss the general principles involved, because I want to draw attention to two small, though vastly important, points.

The first concerns the prognosis of cancer. In the programme of February 18 from the Christie Hospital and Holt Radium Institute in Manchester, it had clearly been decided that information about the chances of cure of cancer should be given. "What sort of proportion of patients achieve this success?" asked the compère of the programme. "I suppose you want me to talk statistics," replied the director of the Institute. "It depends really on the stage of the disease when the patient is first seen. Advanced cases are one problem, but in early cases of some cancers nowadays we can talk in terms of 75% cure, for others in terms of 50% cure." This didn't fool my wife nor two other women who were there. The Englishman may enjoy putting money on an outsider, but when his life is at stake he doesn't regard evens as a very sound bet. And this knowledge accounts for the fact that even the cancer publicists will not tell the truth about cancer. My view is that until the truth is less harsh it should not be stated on television: if anyone really wants it he can find it in the public library.

The second point concerns treatment. At the end of the programme the compère, speaking of modern *x*-ray therapy, said to his unseen millions, "There could be no more comfortable and harmless way of treating any disease than by *x* rays." He may thank his sex that he will never experience three vaginal insertions of radium and three or more weeks of high-voltage *x*-ray therapy to the lateral pelvic walls. Those who are so anxious that a huge number of people should know all about a treatment which they are never going to have should also have the guts to say to them, "This is the hell of a treatment, but at present it is the best there is."—I am, etc.,

London, W.1 MICHAEL HARMER.

SIR,—Dr. Charles Fletcher writes (*Journal*, February 22, p. 456), "I cannot defend the present series, for, like you, I have not seen them as they will appear." From this sentence one can only deduce that Dr. Fletcher is in some way connected with the production of these television programmes on disease. If this be so, then his angry outburst against your leading article (*Journal*, February 15, p. 388) is the more understandable, and I trust that he will also be the more ready to listen to those of us who hold somewhat different views. And whilst I must agree with Dr. John Fry's remarks, also in your February 22 issue (p. 456), concerning the undue emphasis on disease, hospitals, and research, I find myself gravely concerned by some of his other statements. Thus, Dr. Fry writes: "The public should be encouraged to discriminate between good and bad medicine, and in this proper instruction is important." What exact form of instruction is Dr. Fry contemplating or advocating in this connexion? Are we to veer sharply from the Scylla of disease education to the Charybdis of official homilies on "Ideal General Practice," "Health Centres," "Why Your Child's Tonsils should be Preserved," "The Fate and Function of the Foreskin," and other such delectable subjects? Dr. Fry further states that "television is here to stay, and *all our past ideas and ideals must be made to fit in with it*" (my italics). This is surely putting the cart before the horse, and one can only hope that this startling statement is due to an error in transcription. Surely what Dr. Fry really meant was "television is here to stay, but it is a medium which must be used responsibly and made to fit in with our ideas and ideals."

It is not uncommon for pronouncements about medical education of the public to be prefaced by such remarks as "In this Scientific Age the public has a right to know." From this fallacious premise stems most of the misguided effort behind such programmes as you have critized. Certain it is that the individual person has both the freedom and the right to acquire knowledge about almost any subject in which he is interested. If determined enough (or, as some would think, misguided enough) to learn about certain diseases he can get any medical textbook he wants from his public library. Furthermore, if he is unwilling or unable to search out information for himself, he can write to such magazines as *Family Doctor* and have his question answered by a doctor. However much some may disapprove of such publications, it is at least probable that any written answer will be couched in carefully chosen language suitably adjusted to the individual questioner.

Doctors themselves are constantly required to answer questions, but any doctor who is faced with the day-to-day problem of explaining illness and disease to patients and their relatives is frequently humbled by the failure or miscarriage of his efforts. Alas, this can be all too true even when addressing highly educated and well-balanced individuals; how much more difficult it is when dealing with the less well educated, the frankly ignorant, and the ill-balanced. By contrast to this, the would-be educator on radio and television is dealing with a vast audience of millions of people of widely different age, intelligence, education, social background, and mental stability: surely a formidable prospect. To attempt disease education of such a huge and unselected public certainly displays the craziest ignorance of the problems with which we are faced. Even to plan a programme of less emotional content on, say, the scientific background of medicine would be a formidable undertaking.

It is not difficult to see why some of the keenest supporters of these programmes are drawn from the ranks of doctors, their wives, and their more intelligent patients. For people of this type such programmes may provide good entertainment, and they might even have some educational value for the busy G.P. or the specialist who does not practise the specialty depicted. People in this category constitute an extremely small and unrepresentative cross-section of the population. They are, most decidely, *not* the people for whom these programmes were designed. Such matter is not

televised for the edification of an educationally *élite* and exclusive audience; the point at issue is that matter of a highly technical, personal, somewhat emotional, and sometimes sensational nature is being dished out indiscriminately to a mass audience. The impact upon such an audience is hardly touched upon by your medically qualified correspondents, but it does seem to be ably expressed by a layman, Mr. W. G. Stitt-Dibden (*Journal*, March 1, p. 516).

By all means let us have some simple programmes on good health or the basic sciences, but Heaven protect the public from the enthusiastic large-scale medical educationist. At best he is an idealist who firmly believes that he knows what is good for the public, and that the public is entitled to "the facts"; at worst he is a sheer medical adventurer with an eye to the main chance of advertising himself or the institution in which he works.—I am, etc.,

London, W.1. REGINALD S. MURLEY.

SIR,—Those who have seen the guilty stares of members of the public gathered round the victim of a street accident must know the unkind fascination which a mutilated human form excites in people. The lust for such sights is greater than any desire to help, sympathize, or learn. Are those same persons likely to be moved by any quite different sentiment when they are invited to witness the cold-blooded infliction of trauma by a surgeon? Can we not recall that, as students, we were emotionally disturbed, rather than intellectually engaged, when first we saw scalpels parting the flesh, an amputated limb in a corner of the theatre, a corpse, a necropsy, a convulsion, a psychotic patient? It was only conditioning and a serious need to learn, surely, which weaned us from mere fascination and led us to more useful attitudes to disease. With this experience behind us, how can any of us believe that disease is healthy entertainment for the masses?

Any doctor who discusses symptoms with a lay friend feels the need to pick his phrases carefully in accordance with the particular anxieties and misapprehension revealed in his friend. Naturally, the effect of a standard pattern of explanation on a mixed audience will be good in some and bad in others; mass inculcation of many items of medical knowledge is a crude practice—a badly designed experiment conducted without hope of readable results. And the public does not expect us to take part in experiments on human beings, except in desperate circumstances. Many will consider it unfortunate that we already have to ask patients to sacrifice some of their privacy to meet the very real need of medical students. It is an insult to any patient to have present anyone whose place is not either to assist or to learn his profession. The general public have no such cogent need to be present. Those of us who ask patients, as patients, to appear before the public for any purpose that can be construed as "entertainment" are abandoning a tradition which we owe it to the sick, and to the dignity of the profession, to preserve jealously.

It has been suggested that prospective hospital patients need to be reassured about the skill and care with which they will be treated. What cant! Do they need to see engineers immersed in their calculations before they can cross a bridge confidently?

The emotional factors which divide the profession on this issue are easy to identify. Some see their privileged position in relation to patients being jeopardized. It *is* a privilege to know another's personal affairs; and it *does* give satisfaction to know that we are distinguished in this way from others. Provided that we serve diligently in exchange for that distinction, it is a useful indulgence all round. On the other side, there seem to be those who are anxious to profess an overwhelming concern for the "rights" of the anonymous general public, the owners of the Health Service, etc. I am expressing a personal view when I confess that I am suspicious of all such champions of the public in their professions of universal solicitude. Their concern is so like that of politicians. I find more convincing a loving concern and sympathy for the individual, going beside an ability to tell the masses to mind their own business. I believe also that the public, as individuals, find it more convincing.—I am, etc.,

Radlett, Herts HAROLD B. HEWITT.

SIR,—I do not wish to enter the debate on the desirability or otherwise of regaling the public with details of the "mystique" of hospital practice. But the *title* given to the present series of television programmes is surely deplorable.

Your Life in Their Hands conjures up to the lay mind visions of tense dramatic scenes, of split-second decisions, crisis, rescue from the brink of the grave, etc. In fact the title appears to have been chosen to attract the more morbid and sensation-seeking type of viewer and to foster the fears which the programmes themselves are allegedly designed to allay. Engine-drivers and airline pilots also have "lives in their hands," but would the intending passenger find it soothing to be reminded of this aspect of the situation as he embarked on his journey? Perhaps the choice of such a histrionic title throws some light on the real intentions of the B.B.C. I wonder who was responsible for it?—I am, etc.,

Quarndon, Derby. WINIFRED L. TURNER.

Television Casualties

SIR,—I took down the following: "I know I am very foolish, doctor, but since I saw that programme on television I have had difficulty in swallowing and can't sleep at all." For 20 years I have been helping this woman along, and now members of my own healing profession have come between me and my patient and made the job more difficult. Since Hippocrates, we have tried to help the weak and left the strong to look after themselves. All this is now reversed. The healthy must be educated, and if a few weaklings are damaged it is regrettable but justified.

Before we give way to anger, however, let us remember that T.V. personalities are not only rich but rare. Is there not just a chance that a new star may be discovered—a medical Pickles, a nursing Barnett, a radiographing Harding? Should anything, even the welfare of the weak, be allowed to interfere with the march of progress? Would it not be better for stomach powders to be guaranteed by a fully qualified practitioner? Let us not be blinded by old-fashioned prejudice. There is still the gynaecological out-patients to be viewed. Having seen the heart, are we to be denied the cervix?—I am, etc.,

London, N.W.4. R. W. COCKSHUT.

SIR,—I feel that I must place on record my anxiety over the showing of surgical operations on T.V. Far from a so-called desire to educate the public, the only outcome of such a programme has, in my experience, been to produce fear, alarm, and the television "casualty."

Following the B.B.C. showing of the heart operation on February 25, I saw four patients who fainted whilst watching the film. One of these patients, a woman, fainted and fell face first into an open fire, sustaining burns to her face and hair; catastrophe was averted only because her husband, fortunately present at the time, managed to pull her clear before any further damage was sustained.

Warning people of nervous temperament beforehand not to watch the film only has the similar effect of the X certificate in horror films, which apparently seem to attract a very large following. In my experience, the most sturdy and balanced of people have been known to faint on watching their first surgical procedure. Let us protest most vigorously against future such programmes, publicly shown, as it seems to me that their organizers seem to use such stunts only to attract the larger viewing audience.—I am, etc.,

Mitcham. TREVOR SILVER.

"The Unknown Seed"

SIR,—Your leading article in your issue of February 22 (p. 449) referred to the Woman's Hour broadcast "The Unknown Seed" with great unfairness. The writer did not simply express an idea which would be acceptably fair, but tried to colour his readers' judgment by a sneering tone and by the false use of emotionally changed words: " . . . to fortify the public taste for the morbid and sensational," or " . . . doctors lending their private consulting-rooms for this kind of public entertainment." Such phrases may possibly be justified for other items, but they were entirely out of place in this context. Your leader writer is entitled to his opinion (which I personally consider oddly archaic), but he should know better than to use discreditable techniques of vocabulary play instead of reasoned argument.

Listening to this programme, I found it presented with skilled reserve, and, I might add, a certain "ladylike" caution. At its onset the announcer explained how long the item would last, so that any who wished to avoid it might time their switching off. The subject was topical, and it was much more intelligently treated than it had been by the majority of newspapers. Pros and cons were given equal weight. It was an entirely justifiable subject of interest to any thinking woman, and its decent handling was such that a morbid-sensation-seeking listener would have been disappointed. The doctors (anonymous, of course) spoke gravely and reasonably. The gibe that this was contributing to "a kind of public entertainment" was obviously undeserved. This deliberate polemic misuse of words is just not worthy of a scientific journal.—I am, etc.,

Cambridge. A. S. PLAYFAIR.

Hypoglycaemia and the Mind

SIR,—I was interested in Dr. K. M. Hay's letter (*Journal*, February 8, p. 341) and agree wholeheartedly. I fail to see, however, the rationale of a high protein and *low* carbohydrate diet.

Whilst realizing that a *high* carbohydrate intake will produce an increased supply of insulin which in turn will cause a fall in blood sugar, surely a normal carbohydrate intake is desirable. As a migraine sufferer myself, I can fully endorse that long periods without food whilst energy is being expended certainly precipitates an attack.—I am, etc.,

Chigwell, Essex. CONSTANCE P. F. THOMAS.

Carcinoma of the Breast

SIR,—Your leading article on breast carcinoma (*Journal*, February 1, p. 269), whilst presenting current practice, was too superficial to be fully instructive, nor did it give a true picture of the confusion reigning over the disease.

The problems evolve from the doubt whether breast carcinoma is in fact ever cured and the suspicion that improvement in survival figures results from earlier attendance for treatment before many blood-borne metastases have occurred. Statistically Boag[1] has shown that there is little evidence that more than 10 to 15% of patients are permanently cured, for his mathematical approach reveals a steady death rate from disease after correction for deaths from other causes. Long survival is well known, but examination of the early cases (Manchester Stage 1 and 2) treated in Birmingham during 1936 to 1939 reveals that 85% have died, only 6% of the deaths being attributed to any cause other than breast cancer. The inadequacy of surgical removal is seen in cytological studies made prior to wound closure after radical mastectomy, when a high proportion of washings show free malignant cells. The similar overall results obtained at different centres using widely differing techniques are a reflection on modern treatment methods; within the United Birmingham Hospitals series[2] of 4,757 breast carcinomata the results of the radically inclined surgeon differed quite insignificantly from the more conservative. Study of the pathological anatomy shows that nearly 50% of conventional radical mastectomies cannot cure, as 48% of the patients have involved internal mammary nodes[3]; indeed, Wangensteen,[4] employing the super-radical operation, has shown that either the internal mammary chain or the supraclavicular nodes are involved in 60% of cases showing axillary node involvement.

If the influence of surgery on survival is difficult to assess, equally so is the contribution of radiotherapy, for while surgery fails through the presence of conventionally unapproachable local spread radiation fails for lack of sensitivity. Radiation failure is, however, rather more obvious and neither method affects remote metastases. In the Birmingham series it was found that irradiation of the chest wall, axilla, and supraclavicular fossa added nothing to the 5-year survival rate when histology showed no involved nodes in the axilla. However, there was apparently a slight improvement when cases with axillary node involvement were irradiated.

Apart from a very minor change in the survival rate, the only other fact emerging to support the use of radiation as a post-operative measure was a small reduction in the number of patients developing local recurrence. There was, however, a marked increase in the number of patients with distal metastases in the irradiated groups, a seeming contradiction. Whilst the improvement in survival rate may be attributed to radiation, the "mean age" columns probably contain the true explanation, for not only is there a marked difference in the mean ages of the irradiated and unirradiated groups when treated, but the mean age of the 5-year survivors falls by 1.6 years in the unirradiated groups but only by 0.3 and 0.6 years in those given post-operative treatment. One must conclude that the unirradiated groups contain a high proportion of older patients of limited life expectancy dying of other causes before the fifth anniversary, or unable to survive with metastatic disease. Even with the large numbers involved the proof that radiation contributed to the improved survival rate is still lacking.

Birmingham Series, 1936–1949

	No. of Cases	Mean Age at Treatment	5-year Survival Rate (%)	Mean Age of 5-year Survivors	Local Recurrence* (%)	Distal Metastasis (%)
Radical mastectomy; nodes negative ..	359	55·4	66·8	53·8	15·7	30
Radical mastectomy plus irradiation; nodes negative ..	350	52·2	67·3	51·6	9·7	32·5
Radical mastectomy; nodes positive ..	260	57·0	28·3	55·4	22·9	44·0
Radical mastectomy plus irradiation; nodes positive ..	548	52·3	32·7	52·0	18·6	62·7

* Local recurrence is defined as return of disease on chest wall, axilla, or supraclavicular fossa.

The position regarding ovarian suppression is admittedly confusing. The survival rate of the pre-menopausal patient is so much lower than the post-menopausal that it would indeed be surprising if an induced menopause did not improve the prognosis. There is unpublished evidence in at least one centre in the country indicating a real improvement in the survival rate at five years when an irradiation menopause is induced as part of the initial treatment. (Radiation is a satisfactory alternative to oophorectomy and deserved comment in your leading article, for, excepting the slight delay before the physiological menopause appears, *x*-ray suppression of ovarian function is equally effective.) On the other hand, where ovarian function continues, pregnancy does not appear to be so unwise, for, in the Birmingham series, of 32 patients who became pregnant after radical mastectomy, 75% survived five years compared with 35% in a similar group who did not.

There are good reasons to question whether in breast carcinoma it is good advice to advocate adherence to "the well tried and trustworthy methods." To advise the continued application of a method which in at least half the cases cannot cure, in many must disseminate malignant cells over the chest wall, and at the best palliates at the cost of mutilation, we should require more than a respect for the practice of our forerunners.

In spite of the considerable weaknesses of the radical operation, it may be that this operation by expeditiously removing a mass of metastasizing tumour does more good than harm, but so far no convincing series free of the taint of selection has yet appeared. No series has yet shown beyond reasonable doubt that pre- or post-operative radiation convincingly improves the survival rate. Our personal views expressed above convince us that there is an urgent need for an investigation on the broadest possible basis to determine the optimum management of breast carcinoma. We envisage a scheme very much wider than local mastectomy with irradiation versus radical mastectomy. It should include a study of the factors which may influence the activity or otherwise of breast tumours and their metastases as well as prospective study of the treatment of "operable" and "inoperable" cases. It is to be hoped that the Medical Research Council as the most appropriate body will pursue the matter.—We are, etc.,

W. H. BOND.
P. B. KUNKLER.
J. A. H. WATERHOUSE.

Birmingham, 15.

REFERENCES

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2 *United Birmingham Hospitals Annual Cancer Report, 1957*, **111**.
3 Handley, R. S., *Proc. roy. Soc. Med.*, 1952, **14**, 565.
4 Wangensteen, O. H., *Proceedings of the Second Int. Cancer Conf., Cincinnati*, 1952, **1**, 230.

Skia Necrosis from L-Noradrenaline

SIR,—In their article on the use of pressor agents in shock in myocardial infarction Drs. O. Garai and K. Shirley Smith (*Journal*, February 1, p. 247) again emphasize the potential dangers of leakage of L-noradrenaline into the tissues adjacent to the site of injection; local pallor may be succeeded by skin necrosis.

Recently Dr. L. Pelmer[1] has described the use of piperoxane hydrochloride as a measure to counteract these effects. The method consists of multiple subcutaneous injections about the vein with a solution of piperoxane hydrochloride in a dilution of 5 mg. in 20 ml. of normal saline. The amount required varies from 20–30 ml. and is followed by a quick return of the skin colour to the ischaemic area. The method is free from danger. Piperoxane elevates the blood pressure only in the presence of a phaeochromocytoma. The author also refers to the use of hyaluronidase with phentolamine, but from his experience considers that the hyaluronidase may produce a widespread diffusion of both the L-noradrenaline and the vasodilator and so lead to a further increase in the ischaemic area.—We are, etc.,

P. DUTTON.
R. E. FORGIE.

Burnley, Lancs.

REFERENCE

1 Pelmer, L., *J. Amer. med. Ass.*, 1957, **165**, 444.

Intrinsic Factor

SIR,—As Drs. J. B. Stokes and W. R. Pitney (*Journal*, February 8, p. 322) point out, there are two points of practical importance relating to the use of heterologous intrinsic factor. The first and most important is that as a general rule oral preparations of vitamin B_{12} and heterologous intrinsic factor have no real place in the treatment of pernicious anaemia because of the variability and unreliability of results. This has been shown in a trial of one such preparation in a large series of patients.[1] Where serial microbiological assays show that serum vitamin B_{12} levels are kept within normal limits by this form of treatment it may be used, but this is seldom a practical proposition.

The second point is that heterologous intrinsic factor may give "false negative" results in absorption studies with labelled vitamin B_{12}. I have encountered this phenomenon in a patient with a post-gastrectomy megaloblastic anaemia who had not previously received heterologous intrinsic factor. There is also presumptive evidence of refractoriness in the report by Blackburn *et al.*[2]—a previously untreated case of pernicious anaemia which failed to respond to oral vitamin B_{12} and heterologous intrinsic factor but responded to parenteral vitamin B_{12}. These cases suggest that the phenomenon is not invariably a result of previous treatment with heterologous intrinsic factor as Drs. Stokes and Pitney assume. Investigations carried out at the Western Infirmary, Glasgow, along with Dr. John Wallace and Dr. John Anderson, have shown that the phenomenon is not related to blood group or secretor status, and, like Drs. Stokes and Pitney, we have not found evidence of a circulating antibody.—I am, etc.,

J. F. ADAMS.

Glasgow, W.1.

REFERENCES

1 Adams, J. F., *Scot. med. J.*, 1957, **2**, 151.
2 Blackburn, E. K., Cohen, H., and Wilson, G. M., *Brit. med. J.*, 1955, **2**, 461.

Halothane Concentration

SIR,—Anaesthetists who use halothane will know that its effects depend markedly on the concentration used. Precise control is only possible with a temperature-compensated vaporizer, and this is expensive. Trichlorethylene bottles may be calibrated by the makers of halothane, but only for a predetermined temperature (20° C.). It is thus advisable to insert a thermometer through the cork of the bottle, which I have done. If fresh gas-flows of 8 litres per minute or more are used, the temperature soon falls to 15° C., but not with flows of 4 litres. My technique with these calibrated bottles is therefore to use an 8-litre flow until the temperature falls to 20° C.; the flow is then reduced to 4 litres per minute and a modified Waters canister,[1] which fits into the standard semi-closed circuit (Magill attachment) of a Boyle's machine, is used. Alternatively, circle absorption may be used. In this way a known percentage of halothane is delivered, which has some advantages.

It is, however, quite a simple matter to calculate the percentage of halothane delivered from any type of vaporizer if a fixed fresh gas-flow is used and the rate of halothane vaporization is observed; the latter is easy with graduated bottles; otherwise measured volumes of halothane should be poured into the vaporizing bottle. The makers of halothane inform me that 1 c.c. of halothane liquid forms 227.5 c.c. of vapour under working conditions (20° C. and 760 mm. Hg). Thus some simple tables can be worked out (see Table).

Fresh Gas-flow litres/min.	No. of Minutes for 1 c.c. of Halothane to be Vaporized	Percentage of Halothane Delivered
2	2	5·68
2	4	2·84
2	8	1·42
2	10	1·13
2	20	0·56
4	2	2·84
4	4	1·42
4	8	0·71
8	1	2·84
8	2	1·42
8	4	0·71
8	5	0·56
10	1	2·27
10	2	1·13
10	3	0·75

Alternatively the following methods may be used:

Rough Method for High Fresh Gas-flows.—Using a 10-litre fresh gas-flow, observe how many c.c. of halothane liquid are used during exactly 10 minutes. Multiply this by 0.227. The result is the average percentage of halothane delivered during the period. Alternatively, use a fresh gas-flow of 8 litres for exactly 12½ minutes—the result is the same. As the temperature of the halothane will have fallen, the concentration at the end of the period will clearly be lower than at the start.

Accurate Method for Low Gas-flows.—The temperature of the halothane is set at 20° C. before starting (e.g., by using a high gas-flow). A 4-litre flow is now used, and the quantity of halothane in the bottle noted. After 25 minutes the quantity of the halothane used (in c.c.) is noted. This figure multiplied by 0.2275 gives the percentage of halothane. (The volume of halothane vapour in the gas-mixture is so small that it does not materially affect the calculation.)

It will be found that on Boyle's machines the same types of trichlorethylene bottles deliver very different concentrations at a given setting of the lever and plunger. For example, on one machine at a certain setting and gas-flow 1.13% was delivered, while from another apparently identical bottle 2.5% was delivered. The method is also valuable for checking calibrated bottles, as the concentration delivered will be greatly altered if the U-tube is accidentally displaced by quite a small amount. The same method may also be used for calculating percentages of trichlorethylene vapour. 1 c.c. of trichlorethylene forms 248 ml. of vapour; the remaining calculations are the same (i.e., multiply by 0.248 in the two methods above).

Lastly, I have heard that some anaesthetists plug Rowbotham's bottles into circle absorption units. Apart from any other consideration, this is inadvisable, as there is high resistance to gases passing through these bottles, owing to the small ports. Patients should not be made to breathe through these bottles spontaneously, as they were not designed for the purpose.—I am, etc.,

Chislehurst, Kent. JOHN BULLOUGH.

REFERENCE

1 Bullough, J., *Anaesthesia*, 1957, **12**, 354.

Stiff-man Syndrome

SIR,—Having read with interest the article by Dr. Richard Asher on "A Woman with the Stiff-man Syndrome," in the *Journal* of February 1 (p. 265), I am prompted to mention the following case history, which, in view of its rarity and its similarity to the one described by Dr. Asher, may be of interest to your readers.

A 45-year-old physician was admitted to the hospital in New York where I was receiving postgraduate training, with symptoms of severe spasm of the back muscles and both lower extremities. He and his wife and children had come to the U.S.A. in 1943, having succeeded in escaping from racial persecution by the Germans. During his first few years in the States he had gradually become incapacitated and unable to practise medicine, and had finally been rendered bedridden because of spasmodic contractions of the lower limbs and back. Before arriving in America he had apparently been in good health, with no complaints. The course of events after his admission to hospital in 1951 was as follows.

The muscle spasms were fully investigated from every angle, as were the systems throughout the body. Complete and frequent blood pictures and urine studies were made, as were also cerebrospinal fluid analyses. *X*-rays of all the skeletal structure were taken. Muscle biopsies and electromyograms, including faradic and galvanic testing, were carried out; also neuroradiological investigations including complete myelography in view of the possibility of gross disturbances of the central and peripheral nervous system, but these proved negative. The possibility of parathyroid tumour was considered, as were also hypercalcaemia and hypocalcaemia, but blood calcium and phosphate studies were found to be normal.

The fact that the patient was a member of our own profession increased interest in the case, and his hospital records became voluminous. Many specialists and consultants from the divisions in various departments of medicine and surgery, including anaesthesia, neurology, psychiatry, rehabilitation, and physical medicine, reviewed the case, and in the minds of all of them the same diagnosis kept recurring—namely, gross hysteria—which was a fairly reasonable one in view of the negative results of all the extensive investigations. What baffled everybody, however, was to explain the physiology and pathology of the explosive "titanic" and "tetanic" nature of the spasms (as similarly mentioned by Dr. Asher). Neurologically no abnormality was discovered at any time. The spasms, which appeared to be initiated by even slight emotional upset, and at times to be without any obvious cause, gradually increased in frequency and severity during a period of several months. Finally, the extremities and the back muscles became so rigid that a position of opisthotonos was reached in each successive spasm. Before and during the attacks the patient was always extremely agitated, greatly distressed, pale, shocked, perspiring freely, and apparently in great pain.

During one such spasm the neck of the right femur snapped, *x*-rays revealing a subcapital fracture. He was taken to the operating theatre, and during the operation the surgeon drew the attention of the anaesthetist to the fact that he was having trouble with local spasm of the muscles and asked for deeper anaesthesia. The anaesthetist admitted that he too was having difficulty in getting sufficiently deep anaesthesia. Eventually, a Smith-Petersen pin was satisfactorily inserted and checked by *x*-ray. On the way back to the ward, however, the patient had another spasm on the stretcher, and subsequent *x*-ray revealed that this had bent the pin. He was returned to the operating theatre and another pin was inserted. A week later, during a further severe spasm, he fractured the neck of the left femur. This was also pinned and remained intact. From then on he was given more frequent doses of pethidine hydrochloride, together with other sedatives and muscle relaxants, to help in reducing the spasms and easing the accompanying pain. No further fractures occurred, but his condition remained a difficult problem of medical and nursing management, and, so far as I was concerned, until I read Dr. Asher's article, this very rare syndrome was one without a title to the entity.—I am, etc.,

Brentwood, Essex. DESMOND C. J. O'CONNOR.

Anoxia in Pulmonary Emphysema

SIR,—Although one cannot expect the author of your annotation "Neurological Aspects of Pulmonary Emphysema" (*Journal*, February 1, p. 272) to be fully conversant with the literature, I think it is unfortunate that the most interesting effects of severe anoxia on the central nervous system[1] are not mentioned and those that are are attributed to CO_2 retention. Furthermore, to say of the neurological complications that "recent studies . . . have clearly demonstrated that they arise from raised intracranial pressure consequent upon CO_2 retention" is not true.[2]

But to advise the use of 5% CO_2 in oxygen for relief of the anoxia in emphysematous patients suffering from a chest infection is to make CO_2 narcosis certain and a trip to the Old Bailey likely.—I am, etc.,

Enfield, Middlesex. THOMAS SIMPSON.

REFERENCES

1 Simpson, T., *Lancet*, 1957, **2**, 105.
2 Westlake, E. K., Simpson, T., and Kaye, M., *Quart. J. Med.*, 1955, **24**, 155.

Coincidental Sinusitis

SIR,—During these winter months much of my time has been occupied in treating upper respiratory diseases. It is essential to treat most of these cases even if treatment may be only prophylactic, as most general practitioners would agree. In an endeavour to restrict the quantity of antibiotics that I prescribe, I have been using the sulphonamides. In children particularly, one tends to overlook the fact that they may have a coincident sinusitis which apparently does not respond to the sulphonamides given for the respiratory infection. Ebbs[1] has stated that in 30.6% of a series of necropsies in children pus was observed in one or more of the sinuses. In no case had this condition been observed before death. Brown[2] reported that of 100 rheumatic children all suffered from sinus infection. Bronchiectasis undoubtedly follows sinus infection early in childhood. As a result, I have been convinced from my own experience that intranasal treatment with a locally acting sulphonamide should be given at the same time as treatment by mouth. I have been prescribing sulphaethylthiadiazole per os, as it is, in my opinion, a drug free from side effects; and intranasally I have had patients instil micro-crystalline sulpha-

thiazole, a preparation containing sulphathiazole with a crystal size of approximately 1/1,000 of the normal, which is slightly acid and fluid. This overcomes the disadvantage of sulphonamide solutions intended for topical use which are necessarily alkaline and may irritate the nasal mucous membranes.

From the cases I have treated, provided the instillation into the nose has been efficiently performed, I am convinced that the upper respiratory infection clears more rapidly and the risk of reinfection or continued infection from the nose is limited. I have never myself been satisfied that the intranasal sulphonamide has been the cause of sensitization to any degree. I feel sure that, because of this minor risk, to ignore the nasal and sinus element when treating bronchitis associated with coryza is a mistake.—I am, etc.,

Farcham, Hants. E. P. J. MORAN.

REFERENCES

1 Ebbs, J. H., *Brit. med. J.*, 1938, **1**, 385.
2 Brown, E. E., *Arch. Pediat.*, 1951, **68**, 565.

"Nomen Proprium"

SIR,—The opinions expressed by Dr. D. Saklatvala and Dr. A. P. Cawadias (*Journal*, December 28, 1957, p. 1547) and Dr. H. Ucko (*Journal*, January 4, p. 40) are much less moderate than those put forward in our original letter (*Journal*, December 7, p. 1366). All these correspondents appear to be so obsessed with their own viewpoints on the use of the term *nomen proprium* that they failed to give us any credit for our statement that "in some instances there are no objections; indeed there may be advantages to be gained" by its use.

Dr. Cawadias seems to imply that we do not support the principle of carrying out the instructions of the prescriber embodied in the term *nomen proprium*. We would urge him to re-read the final sentences of our letter, which emphatically deny this implication. In answer to Dr. Ucko, of course leaflets can be and are removed from original packings *prior to dispensing*. But they will not be removed—and this is the point we made—*prior to direct purchase*. To suggest, however, that the risk of a drug being used when it may have become inert could be avoided by having such drugs issued in original containers would in many cases nullify the effect of removing leaflets because of the information given on the manufacturer's label.

In our view none of these correspondents has shown that there are not two sides to this question, and we maintain that the points we made merit a more dispassionate reading that was accorded to them.—We are, etc.,

C. WILSON PECK,
Chairman.

London. G. BRYAN,
Hon. Secretary.
Association of Teaching Hospital Pharmacists.

Informal Admission of Mental Defectives

SIR,—Please may I be allowed to comment upon two letters which have appeared in your correspondence columns, and which imply criticism of my views on the above subject, which you were previously kind enough to publish in the *Journal* of February 8 (p. 338)?

It is quite clear, as Dr. L. J. Segal points out in his letter (*Journal*, February 22, p. 459), that it is not necessary in every case where hospital admission is required for a mentally defective patient to have legal powers of detention. The difficulty arises in assessing with any degree of certainty for which cases legal powers of detention are not necessary. In this context, the severely handicapped mental defectives present the smallest problem, as Dr. Segal intimates, but some legal sanction might be given for their apprehension should they wander away from the hospital grounds. As the degree of defect becomes less, at what stage does returning a straying sheep to the fold become an outrageous encroachment upon the liberty of the subject? This point would have to be decided by the medical officer, who might later receive little sympathy in court when accused of an "unjust apprehension."

Dr. Segal goes on to suggest that informal stay in hospital for higher grade mental defectives may often be inappropriate, and here I think that we are in complete agreement. I merely contend that it is virtually impossible to state confidently for which of such patients legal formalities can reasonably be waived. As he says, the ideal way to obtain hospital treatment for a mental defective is on an informal basis, but I am not convinced that it is the practical way.

In his general attitude, and in his criticism of the review of patients at intervals by the visiting justices, Dr. Segal is joined by Dr. E. Fischer (*Journal*, March 1, p. 518). That this review should be an embarrassment to relatives of patients is obviously to be regretted, and some modification of the process is clearly indicated if such is the case, which is quite likely, although I have never personally come across this difficulty. The value of this periodic review by the magistrates as a safeguard to both patients and hospital authorities must nevertheless be borne in mind. Finally, Dr. Fischer points out at the end of his letter that it is not required, according to the circular, to discharge from Order patients who in the opinion of the medical superintendent should remain under Order. Yet Dr. Segal states that, "after all, de-certification still rests with the Board of Control." Is it then possible that medical superintendents will be asked to retain some patients informally, for whom they themselves consider that informal stay in hospital is inappropriate?—I am, etc.,

Ash Priors, near Taunton. M. P. NELSON.

Obscure Abdominal Pain

SIR,—Mr. F. R. Brown (*Journal*, February 22, p. 462) is surprised at some of my diagnostic mistakes, but I must point out to him that I never said that visceral pain was felt in either the right iliac fossa or the left hypochondrium. I stated that pain in these sites could be a symptom of ailments in the appendix and stomach, and that is so.

Mr. Brown produces a theory to explain where pain should be felt, but, alas, we learn from observation that facts do not always fit into our theories. I am for ever treating flatulent, dyspeptic women who present complaining of a bad heart because they have pain below the left breast, but they are all cured with alkalis. The site of the disease is the stomach, the symptom is in the left side of the chest, and the mechanism may well be pressure on the diaphragm. I have seen lead shot in the appendix cause pain in the right iliac fossa. Mr. Brown will have it that this and the pain of my duodenitis, which has never been in the midline, are both caused by irritation of the parietal peritoneum, for this is the only mechanism by which the pain could be felt in these situations since he rejects the theories of Sir James Mackenzie[1] and Morley.[2] Let us not, however, forget the other extreme of Lennander,[3] who denied that the viscera had any nerves at all and attributed all visceral pain to the parietal peritoneum. One must marvel at the sensitivity of the parietal peritoneum, which can so easily be a source of duodenal pain, and which can cease to cause such pain within a few minutes of the taking of food or alkalis, and yet which, after a gangrenous appendix has burst, may cease to cause pain to such an extent that the patient is lulled into a sense of security which has often proved fatal.

We do not yet understand the mechanism of much of our pain. The pain caused by the protrusion of an intervertebral disk pressing on the dura mater can be either central or to one side according to which part of the dura is pressed upon, and this can be shown at operation under local analgesia. A similar protrusion can cause pain in the back and umbilicus simultaneously. A posterior protrusion of a lower cervical disk can cause pain at the tip of one scapula which is located in the seventh thoracic dermatome, and under manipulative reduction this pain together with the accompanying local tenderness can be made to pass successively through all the dermatome above until it reaches the midline at the lower cervical vertebrae before disappearing.

I do not think that Mr. Brown will ever explain the phenomena described in the last paragraph if he persists in

fitting his observations into the procrustean bed of a theory learnt in his preclinical studies. The sanctity of Galen caused centuries of stagnation in medical science, and it is only by careful observation and criticism that we shall unravel the mysteries of the microscopic anatomy of the nervous system, a system of which we as yet know only a very small proportion, consisting mainly of the macroscopic anatomy.—I am, etc.,

Brampton, Hunts. R. T. D. FITZGERALD.

REFERENCES

1 Mackenzie, J. (1912). *Symptoms and Their Interpretation*. London.
2 Morley, J. (1931). *Abdominal Pain*. Edinburgh.
3 Lennander, K. G. (1903). *Sensibility of the Abdomen*. London.

First Tuberculosis Dispensary

SIR,—In their letter (*Journal*, February 8, p. 339) Drs. W. Hartston and W. F. Wheeler state that the Liverpool Street Dispensary, founded 1848, preceded Sir Robert Philip's Edinburgh dispensary. It would, however, appear from Davidson and Rouvray's history of the Brompton Hospital[1] that there was an even earlier institution. This was the West London Dispensary for Diseases of the Chest, 83, Wells Street, Oxford Street, which existed round about 1841. Its physicians were Thomas Elliotson and Sir Charles Scudamore, and its surgeons John Carter and Benjamin Travers. When the plans for the Brompton were being drafted, the West London Dispensary, realizing that the proposed hospital would have a much wider scope, discontinued its operations, and in a public announcement generously recommended its patrons to support the new venture. This establishment seems to have carried out the functions of a dispensary as they were understood at the time. By Sir Robert Philip's days it was possible for him to take the wider view that Dr. G. Lissant Cox refers to in his letter (*Journal*, February 15, p. 402).—I am, etc.,

London, S.W.3. P. J. BISHOP,
Librarian,
Institute of Diseases of the Chest.

REFERENCE

1 Davidson, M., and Rouvray, F. G., *The Brompton Hospital*, 1954, p. 8. Lloyd Luke, London.

Thumb-sucking

SIR,—One would expect thumb- (or finger-) sucking to be uncommon in primitive society where oral satisfaction in infancy is likely to be complete. My own observation is illustrated by the following figures, which are the result of questioning the mothers of 75 consecutive children aged 1 or 2 years at child welfare clinics in Kampala. Of the 75 children 21 persistently sucked a digit, in 10 it was the thumb, in 6 the index finger, and in 5 the two middle fingers.

Oral satisfaction is perhaps not quite so satisfactory among Africans living here as it was a few years ago; nowadays about 30% of children are given supplementary bottle-feeds before the age of 6 months. On the other hand, breast-feeding is still far more satisfactory and prolonged than it is in Western countries—the average age for complete weaning from the breast is 12–14 months. That digit-sucking is no modern innovation is shown by Baganda "old wives' tales." It used to be said that if a child sucked his thumb he would kill his father, and this must be prevented by cutting the thumb with a grass and applying pepper. On the other hand, if he sucked his fingers the mother was to be congratulated, because she had a child who would be placid and contented—perhaps this is why we see more suckers of fingers than thumbs! The oldest "old wife" we had the opportunity to question was aged 101 years; she remembered as a child being told about the significance of thumb-sucking, and when she grew up she cut her own children's thumbs when they sucked them. Her grandchildren and great grandchildren, who are personally known to me, were allowed to suck their thumbs, which they did with satisfaction and no ill effects either to themselves or their fathers. In fact nowadays thumb-sucking seldom causes alarm or even annoyance to Baganda parents. And in spite of a relatively high (28%) incidence of the sucking habit, no ill effects are seen. My dental colleagues tell me that deformity of the maxilla is far less often seen here than in Europe.

I wonder how the incidence of digit-sucking here compares with that in Europe. My impression is that among toddlers the incidence here is not so very different from that in Europe and that among this age group the habit is not necessarily associated with psychological insecurity and it seldom leaves any impression on dental development. Perhaps, because the attitude of the African parent is more often one of condolence and amusement rather than of irritation and shame, African children tend to grow out of the habit more rapidly.—I am, etc.,

Kampala, Uganda. H. F. WELBOURN.

Living on a Pension

SIR,—Eighteen months ago you kindly printed a letter (*Journal*, August 4, 1956, p. 304) from me asking for budgets of medical men retired from practice for my book, *£ s. d. of Retirement*. (To an earlier appeal in a previous book only two doctors had responded in 1954.) Your publication of my letter has remedied this completely. Some admirable budgets have now come in. One perfect model I have printed.

But there were others. Incredibly, the most hopeless budgets came from your highly educated profession. Presumably the high pressure at which so many doctors work to-day, coupled with the highly specialized nature of their university training, accounts for this gap in their equipment for living. At the urgent request of medical friends I have even added a glossary of financial, Stock Exchange, and insurance terms at the last moment. Apparently these are Greek to many medical men. Yet to-day many doctors are clearly retiring under the National Health Service's pension scheme on from one-quarter to a half of their incomes while in active practice. This presents a financial problem as acute as that of the axed Service man.

Cannot the B.M.A. arrange a series of short courses in investment, insurance, budgeting, and efficient buying for doctors within sight of retiring age? Certain Service courses of this type are run most successfully for officers about to be retired. The lively problems put at question time show how much such a course means to some officers.—I am, etc.,

Fairlight, near Hastings. CECIL CHISHOLM.

Surfeit of Medical Papers

SIR,—I found an interesting side-light on this correspondence in a book over one hundred years old, *Mémoires d'un Bourgeois de Paris*,[1] written by a Dr. L. D. Véron. Dr. Véron was born on April 5, 1798, and graduated as Doctor of Medicine at the Paris Faculty of Medicine in the year 1823. He did not remain a practising physician all his life and for many years was the director of the Paris Opera. However, he retained his love for his profession, and on page 339 of the first volume of his six-volume *Mémoires* he writes:

"Je lis beaucoup de journaux de médecine; on écrit beaucoup et peut-être trop en médecine. Je lis les comptes-rendus de l'Académie impériale de médecine, de la Société de chirurgie de Paris, de la Société médico-pratique de Paris, de la Société médicale des hôpitaux de Paris, de la Société médicale d'émulation de Paris, des Sociétés médicales des arrondissements de Paris, et j'assiste ainsi de loin à tous les mouvements de la science."

It seems to me, that it is only the high cost of producing journals which prevents the surfeit from becoming a glut.—I am, etc.,

Romford, Essex. LEON M. SHIRLAW.

REFERENCE

1 Véron, L. D., *Mémoires d'un Bourgeois de Paris* (6 vols.), 1853-5. G. de Gonet, Paris.

POINTS FROM LETTERS

Problems of Puberty

Dr. D. S. MAYMAN (Barnsley, Yorks) writes: With reference to the letters of Drs. R. N. B. Byatt and E. A. Knappett concerning masturbation (*Journal*, February 15, p. 397), is there any proof that masturbation is not a normal physiological act?

Obituary

J. G. EMANUEL, M.D., F.R.C.P.

Dr. J. G. Emanuel, consulting physician to the Queen Elizabeth and other Birmingham hospitals, died at the Queen Elizabeth Hospital on March 3. He was 86 years of age.

Joseph George Emanuel was born at Birmingham on June 4, 1871, the eldest son of the Rev. G. J. Emanuel, and was educated at the King Edward's High School there, studying medicine at the Mason and Queen's Colleges. He took the London B.Sc. in 1891, and qualified in medicine by taking the London Conjoint diploma in 1896, in which year he was Ingleby Scholar. He obtained the London degrees of M.B., B.S., with honours in obstetrics, in 1898, and proceeded to the M.D. in 1901. Elected a Member of the Royal College of Physicians of London in 1902, the year in which he was granted the degrees of M.B., B.Ch. of the recently founded Birmingham University, he was admitted a Fellow of the College in 1921. After qualification he held a number of appointments at various London hospitals, including that of resident medical officer at the City of London Hospital for Diseases of the Chest, where, earlier, he had been house-physician. Returning to Birmingham in 1900, he was resident pathologist at the General Hospital for the next two years. From 1902 to 1909 he was physician to out-patients at Queen's Hospital, Birmingham, becoming physician to the hospital in the latter year, and retiring from the staff in 1931 on reaching the age limit of 60. In 1904 he was appointed physician to the Children's Hospital, becoming consulting physician in 1920. During the first world war he served as a captain in the R.A.M.C. at the 1st Southern General Hospital and at the 56th General Hospital in France.

Emanuel had practised as a consulting physician, with a particular interest in cardiology, since 1903, and in 1925 delivered the Ingleby lectures at Birmingham University, taking for his subject auricular fibrillation. A member of the British Medical Association for over sixty years, he acted as one of the honorary secretaries of the Section of Medicine when the Association held its Annual Meeting at Birmingham in 1911, and at Bournemouth in 1934 he served as a vice-president of the same Section. He married Miss Ethel Wolff, daughter of Dr. Alfred Wolff, and she died in 1951. He is survived by his only son, Dr. R. W. Emanuel.

H. W. F. writes: At the time of his death Emanuel was the senior physician of Birmingham, and, although he was in his 87th year, he retained the same carefulness of thought and equanimity of mind which had been characteristic of him throughout his long life. He was a Birmingham man, and he remained a loyal member of the Hebrew congregation, of which his father, the Rev. G. J. Emanuel, had been minister. At King Edward's School gatherings of old boys and in university circles he was a most welcome and enthusiastic visitor. Recently, however, a foot disability hampered his bodily activity, a handicap which, though of grave portent, did not in any way quell his cheerfulness and his kindly interest in all that went on. His experience as house-physician and resident medical officer at the City of London Hospital for Diseases of the Chest for three years under Eustace Smith stimulated him to become a progressive doctor. And from 1900 until 1902 he was resident pathologist at the General Hospital, Birmingham, where his duties were extensive. He made all the post-mortem examinations, he was responsible for the histology of all specimens sent from the operating theatres and from the post-mortem room, and he was bacteriologist to the hospital. At that time the Widal reaction was a daily requisition, for typhoid was rife. In 1900 the pathologist prepared his own media, and this involved the sterilization of broth on three successive days, because sterilization under pressure had not reached the General Hospital. Another responsibility was the special blood count; the importance of leucocytosis as evidence of bacterial infection had just been recognized. Emanuel introduced into Birmingham Ehrlich's tri-acid stain for the differentiation of the various white corpuscles. He was the first in that centre to distinguish "myelogenous" from "lymphatic" leukaemia. In the course of his work he developed a severe infection of the hand, and the resulting septicaemia was nearly fatal.

When Arthur Foxwell was killed in a cycling accident in 1909, Emanuel filled the resultant vacancy of assistant physician at the Queen's Hospital. Recognition of his capacity as a clinician, both as a teacher and as a consultant, grew rapidly. He soon developed special skill as a heart specialist, and he wrote a number of authoritative papers on this subject. His Ingleby lectures on auricular fibrillation were published in book form. He wrote also early papers on the diseases of children and on allied subjects. For some years he was professor of medicine in the University. He was on the staff of the Children's Hospital, the Eye Hospital, and Dudley Guest Hospital. But he was especially proud of his election to the presidency of the Association of Physicians in 1939, when his colleagues in the Midlands insisted that he should occupy that important position on the association's visit to Birmingham. Students and residents found "Wiggy," as he was called, a friend whose manner was free from sarcasm or aloofness—attributes which were not uncommon in those days. When he was a junior he was regarded as rather slow, but when he asked a question or offered an opinion it was realized that his observations went direct to the heart of the matter. This care in speech and thought was associated with sensitive feelings, and he suffered keenly when subjected to hostile criticism. His loyalty embraced each of his interests, his work, his hospitals, and his family. The loss in 1951 of his wife, whom he had married in 1908, was a severe blow. Their only child, Dr. Richard Emanuel, is a physician in London. Two nephews, Dr. Reginald Abrahams and Dr. Frank Gould, are well-known doctors in Birmingham.

W. QUARRY WOOD, M.D., Ch.M., F.R.C.S.Ed. Hon.F.R.F.P.S.

Mr. W. Quarry Wood, consulting surgeon to Edinburgh Royal Infirmary, died in Edinburgh on February 28 at the age of 69.

Walter Quarry Wood was born on September 9, 1888, one of the seven sons of the late William Wood, of St. Boswells. Entering Edinburgh University in 1906, he graduated M.B., Ch.B. in 1911. He was elected a Fellow of the Royal College of Surgeons of Edinburgh in 1914, and proceeded to the M.D. in 1916 and the Ch.M. in 1922, both with gold medals. Quarry Wood's connexion with Edinburgh Royal Infirmary, where he was to do most of his work, began in 1911, when he was appointed house-surgeon to Professor F. M. Caird, Regius Professor of Clinical Surgery, and, apart from a period in the R.A.M.C. during the first world war, he served on the staff of the hospital for 42 years. Appointed assistant surgeon after the war, he became surgeon in charge of wards in 1939 and retired in 1953. In his earlier years he was also assistant surgeon to Chalmers Hospital, and up to the time of his retirement held the post of consultant surgeon to the Border hospitals. A clinical teacher throughout his hospital career, he was for many years lecturer in anatomy in the university and undertook a great deal of research work, particularly on embryology and on the histology and pathology of the endocrine glands. Essentially a general surgeon, he was particularly interested in the surgery of the intestinal tract, on which he made many notable contributions, including a paper with Sir David Wilkie on carcinoma of the rectum with special reference to its spread.

Quarry Wood was elected President of the Royal College of Surgeons of Edinburgh in 1949, and during his tenure of office arrangements were made for reciprocity in the primary

fellowship examination with the other Royal Colleges and, in addition, provision for the interchange of examiners. He represented his College at the 350th anniversary celebrations of the Royal Faculty of Physicians and Surgeons of Glasgow in 1949 and received the honorary Fellowship of the Royal Faculty on that occasion. He became president of the Edinburgh Medico-Chirurgical Society in 1955 and served for two years in that position. For some months Quarry Wood's health had been causing his colleagues grave anxiety, but, typical of the man, he never complained, and continued his surgical work and attended clinical meetings until a few weeks before the end. He will be mourned by a wide circle of his patients and by his colleagues, who have lost a wise counsellor and a true friend. The sympathy of them all is extended to his widow and daughter.—K. P. B.

JOHN CLAY, M.B., B.S.

Dr. John Clay, who was killed in a motor-car accident on February 5, had been in practice in Letchworth for nearly twenty-five years. He was 48 years of age.

John Clay was born on January 24, 1910, the eldest son of Mr. John Clay, consulting surgeon to the Royal Victoria Infirmary, Newcastle upon Tyne. After leaving Cheltenham College he became a medical student at Newcastle and graduated M.B., B.S. in 1932. After graduation he was house-surgeon to Professor G. Grey Turner at the Royal Victoria Infirmary, Newcastle, and, later, house-physician at the same hospital. He then became resident medical officer to the Princess Mary Maternity Hospital at Newcastle, before settling in practice at Letchworth.

C. P. C. writes: The death of Dr. John Clay is a major tragedy for Letchworth and the county of Hertford: everyone in the area who knew him has felt a sense of personal loss. He was at the time driving to the Essex coast, where he had recently acquired a cottage which he hoped to use for his favourite hobby of sailing.

I was indeed fortunate to persuade John Clay to leave his home city and university to enter general practice in the rapidly growing first garden city in November, 1934. From the first it was obvious that he would spend himself to the utmost in the service of his patients and in giving loyal help to his colleagues. In July, 1938, he was appointed to a commission in the R.A.M.C., T.A., and joined his unit for active service on September 1, 1939. He served in France, being one of the last to leave the Dunkirk beaches, then in Madagascar, and again in France and north-west Europe from 1944 until he was demobilized in October, 1945. Quickly attaining his majority, he was promoted lieutenant-colonel in January, 1945. Twice mentioned in dispatches, he was awarded not only the 1939–45 Star, the France and Germany Star, the Defence Medal, and the War Medal, 1939–45, but also the Croix de Guerre. After this distinguished war service, John Clay returned to our practice, bringing with him the wide administrative experience gained overseas. Before the war he was surgeon to the Letchworth division of the St. John Ambulance Brigade, and in 1949 was promoted to area surgeon and, later, to area commissioner of the northern part of the county of Hertford. He held the long-service medal, with bar, and was invested as a Serving Brother of the Venerable Order of St. John of Jerusalem in 1957. He was a keen supporter of almost every sporting and social activity in the town. Elected a member of the Letchworth Urban District Council in 1947, he served as a councillor, as vice-chairman, and as chairman in 1956, and was tireless in his efforts to promote the well-being of the electors. He was an active member of the East Hertfordshire Division of the British Medical Association and had been a member of the executive committee since 1953.

John Clay was a lovable man. Genial, kindly, and sympathetic, he had been called "the ideal general practitioner." He always brought warmth and comfort into the lives of his patients, his colleagues, and his innumerable friends. His presence alone was sufficient to do this, without apparent effort, and we have all suffered a tremendous loss in this most unexpected tragedy. In 1935 he married Veronica Maureen, daughter of Dr. and Mrs. John Murray, of Blackhill, County Durham. She miraculously escaped with minor injuries in the accident which killed her husband. To her and the five sons of the marriage, as well as to his parents, we, the writer and all his friends, send our loving sympathy.

W. R. SPRUNT, T.D., M.B., Ch.B.

Dr. W. R. Sprunt died on February 15 at his home at Berwick-upon-Tweed, where he had been in practice for nearly thirty-four years. He was 63 years of age.

William Rodger Sprunt, whose father was schoolmaster in Forteviot, was born in Perthshire in 1895. He was educated at Perth Academy and at Edinburgh University, where he graduated M.B., Ch.B. in 1923. His education was interrupted by the first world war, for he enlisted in the Royal Engineers in January, 1915, and served as a non-commissioned officer until demobilization in December, 1918. He was wounded in 1916. Dr. Sprunt settled at Berwick-upon-Tweed in partnership with Dr. P. W. Maclagan in 1924, succeeding Dr. Maclagan's father, Dr. C. G. Maclagan. Years of hard and increasing work followed. He was medical officer to the Berwick Infirmary, and parish medical officer until 1948, when he became medical officer to the Greenhaven Home. A regular but not uncritical supporter of the British Medical Association, he was chairman of the North Northumberland Division in 1936–7. In his outside interests he was past master of the Berwick St. George's lodge, vice-chairman of the British Legion, and, in later life, a trustee of Wallace Green Church and a past president of the St. Andrew's Club. A keen fisherman, he enjoyed nothing more than a summer evening on Tweed or Whitadder.

R. H. D. writes: Dr. Sprunt's main interest, apart from his work, began in 1929, when he became medical officer to the 4th battalion of the King's Own Scottish Borderers, Territorial Army. Mobilized in 1939, he was only a few months with his battalion when, on promotion to the rank of major, he joined a field ambulance in France with the 52nd Division. He became lieutenant-colonel in 1941, taking command of a field ambulance, and served in Syria, North Africa, and Italy until 1945. For his work in Italy he was mentioned in dispatches in 1945. On his return to practice in 1945 he rejoined the 4th battalion of the K.O.S.B., retiring under the age limit in 1950, but continuing his connexion with the Army until his death as civilian medical officer to the local depot of his old regiment. It was fitting that his devotion to his community and country should, in 1946, be recognized by his appointment to the ancient office of Sheriff of Berwick-upon-Tweed. He and Mrs. Sprunt performed the duties most acceptably, but his great happiness in the honour was in being Sheriff at the ceremony when the freedom of the borough was conferred on his regiment. All those who worked with Dr. Sprunt and all those for whom he worked have spoken well of him, remembering the honesty, integrity, and kindliness which came from the unswerving faith that guided his life. The deepest sympathy has been felt for his widow, who was in every sense partner of his life and work.

D. H. PENNANT, D.S.O., M.D.

Dr. D. H. Pennant, who was a well-known general practitioner in Pembrokeshire, and a former chairman of the Pembrokeshire County Council, died at his home at Saundersfoot on February 28. He was 67 years of age.

Dyfrig Huws Pennant was born on September 1, 1890, the second son of Mr. William Pennant, of Pontycymmer, Glamorgan, and was educated at Llandaff Cathedral School and at Clevedon College. He began his medical training at

Cardiff and went on to the London Hospital, where he was awarded an honours certificate with a scholarship in clinical surgery. Having qualified M.R.C.S., L.R.C.P. in 1912, he held the appointments of junior house-surgeon and senior gynaecological house-surgeon and senior house-physician at the Prince of Wales's General Hospital, Tottenham, and then became assistant medical officer at the Barnwood House Hospital for Mental and Nervous Disorders, Gloucester. During the first world war he served in the R.A.M.C., and while attached to the headquarters of the Royal Field Artillery in 1917 he was awarded the D.S.O. for conspicuous gallantry and devotion to duty. He was also twice mentioned in dispatches.

After demobilization he returned to Barnwood House Hospital as senior assistant medical officer, but left there in 1920 to settle in general practice at Saundersfoot, Pembrokeshire. He became also medical officer and public vaccinator for the Begelly district of the Narberth union, medical officer to the Post Office, and honorary medical officer to Tenby Cottage Hospital. He was chairman of the South-west Wales Division of the British Medical Association in 1927–8. In 1931 he was granted the Durham degree of M.D. Elected a member of the Pembrokeshire County Council in 1937, he became an alderman ten years later, and was chairman of the council in 1950–1. For three consecutive years he was chairman of the education committee, and he was High Sheriff of the county in 1950–1. From 1948 to 1954 he was a member of the Welsh Regional Hospital Board and chairman of the West Wales mental hospitals group, relinquishing both appointments only because of ill-health. He was also a governor of the National Library and of the National Museum of Wales, a member of the council of the Welsh National School of Medicine, and an honorary life member of the Venerable Order of St. John of Jerusalem. After giving up medical practice he took up potato-farming as a spare-time hobby. At the 1951 General Election he contested Pembroke in the Liberal interest, but failed to win the seat. He married Miss Nan Davies in 1917 and had two sons, one of whom was killed in action in the second world war.

T. R. G. writes: By the exercise of great professional skill and untiring devotion to duty Dr. D. H. Pennant soon built up a reputation that extended beyond the bounds of his own locality. He practised at a time when it was necessary for a country doctor to be an all-round master of his craft, and perhaps the greatest tribute that can be paid to him is to say that he measured up to this high standard. He had a great love for and a great understanding of people, and outside the field of medicine was always ready with sound advice and generous help. He had a great urge to serve the community, and it is not surprising that, in preparation for his retirement, he entered public life by becoming a member of the county council. After his retirement from medical practice in 1948 he gave to the public service the same qualities he had applied to his practice, and within a very short time became a very prominent public figure in the county. He was much loved and will be greatly missed by a large number of his old patients, by the county he served so well, by his colleagues, and, most of all, by his widow and son.

W. J. HIRST, *M.C.*, M.B.

Dr. W. J. Hirst, who was a general practitioner in Birmingham for more than thirty-five years, died in the General Hospital on February 28, aged 83, after a long illness most stoically borne.

William James Hirst was born on April 19, 1874, and was educated at the Yorkshire College, Leeds, graduating M.B. from London University in 1898. After holding the appointments of house-physician at the General Infirmary at Leeds and resident medical officer at the Newark Hospital and Dispensary, he settled in general practice at Moseley, remaining in the Birmingham area for the rest of his life, except for the period of his service in the first world war. In 1918, while serving with the 2/1 South Midland Field Ambulance, he was awarded the Military Cross, the citation accompanying the award reading as follows: "He organized the evacuation of wounded from a village during an enemy attack; he remained behind when the enemy advanced into the village and assisted in removing all the wounded, refusing to leave the village until the last man had been brought in. He has at all times shown great coolness and disregard of danger under heavy fire." A member of the British Medical Association for fifty-four years, he was chairman of the Birmingham Central Division in 1932–3.

A. W. F. C. writes: William James Hirst was a man of great Christian character, inflexible will, and indomitable energy, and in addition he had an absolute humility which was as sincere as it was disconcerting. Not an easy man to know, being rather reticent by nature, he nevertheless had a large practice and not an enemy in the world. He was the despair of locums—especially those newly qualified—for his ordinary work would be four surgeries a day and up to forty visits, year in, year out: he was so much stronger than they—never ill, always patient, never in a hurry, and working into the small hours on most nights. Dr. Hirst loved medicine and all to do with it, and after his retirement regularly visited the skin and dental hospitals, where his services were valued highly. He was a man who seemed to have no fear, and his Military Cross was won because his sense of duty and his Christian principles were unshakable in what was almost a suicide bid to save British personnel in the enemy lines. For many years he was the secretary of the Moseley and King's Heath ward of practitioners, and he proved himself indispensable, for after his health failed and he was unable to attend meetings a vital part of the spirit of these meetings had departed. In his last few years he lived with an invalid sister, but never complained, and though desperately ill chose to remain at home till the last day of his life. Such fortitude is unforgettable. He was a rare person, and all who knew him were the better for it.

T. LEVITT, F.R.C.S., F.R.C.S.Ed., F.R.C.S.I.

The obituary of Mr. T. Levitt was printed in the *Journal* of March 1 (p. 526).

A. B. writes: The untimely death of Mr. T. Levitt has removed from the medical scene of London a remarkable man. He was actuated by high moral principles, and his personal qualities based on sincerity made him the most desirable of friends and the most valuable of colleagues. The keen pursuit of sources of new knowledge was carried out with disregard to his health, without thought for his personal career or for any financial reward. For "Toby" Levitt medicine was a creed and surgery a religion. When remembering the affection for Mr. Levitt of his patients and of his pupils, one can say that he truly practised Swedenborg's motto: "Man is born to live not for himself, but for others."

Mr. RONALD W. RAVEN writes: The constant struggle of a brave soul to reach its goal in the face of great difficulty occasioned by infirmity excites our sympathy and admiration. These are greatly deepened when we witness the final breakdown, leaving the task unfinished. Many of us grieve at the passing of Toby Levitt, who battled bravely on for several years in spite of ill-health which was a constant concern to those who knew him, but about which he seldom spoke. He will be missed by many people who will retain in memory his sincerity and modesty. Who can, forget those searching eyes and smile of comprehension? I have known him for many years and watched his progress with much interest. I was closely associated with him during the last war in North Africa and Italy, and recently when he was a Gordon Jacobs research fellow at the Royal Marsden Hospital. His health precluded him from continuing work as an operating surgeon, but in spite of this disappointment he achieved happiness in a new

sphere of work which was opening out for him. He was intensely interested in endocrinology in relation to cancer, and his life was dedicated to find some of the answers to various problems in this field. He used the Hunterian method; how assiduously he collected the facts (recorded in his note-books in the neatest handwriting), which he proceeded to classify with enthusiasm; and then he made his deductions, which he explained with much lucidity. He was a most acceptable teacher of surgery to postgraduates, and large numbers benefited greatly from his classes. Toby loved life at its best, and never spared himself in the search for knowledge. This included his love of Italian art and architecture, and to appreciate this all the more he took considerable trouble to learn the Italian language. He is not forgotten, for in addition to these memories we treasure he has left his monumental book on diseases of the thyroid gland, which is studied throughout the world. As he was laid to rest on that wintry day the sun was shining—in Thy light he shall see light and find perfect satisfaction in the peaceful contemplation of eternal truth and reality.

A memorial service for the late Dr. J. G. Greenfield will be held in the Church of St. Martin-in-the-Fields, London, W.C.2, on March 20 at 12 noon.

Medico-Legal

CARNAL KNOWLEDGE OF MENTAL DEFECTIVE

CROWN APPEAL TO LORDS DISMISSED

[FROM OUR LEGAL CORRESPONDENT]

On March 6[1] the House of Lords delivered its reserved judgment in the appeal of the Crown[2] from the decision of the Court of Criminal Appeal, which had allowed the appeal of John Shortriggs Head from his conviction at Carlisle Assizes. Head had been convicted under s. 56(1)(a) of the Mental Deficiency Act, 1913, on a charge of having carnal knowledge on October 7, 1956, of a woman who was a mental defective and was at the time on licence from Dovenby Hall Hospital, Cockermouth. The defence was that the woman had never been lawfully detained as a mental defective because the medical certificates which were before the Secretary of State as the basis for his order did not contain any evidence that she was a moral defective within s. 1(1)(d) of the Act of 1913. The Court of Criminal Appeal had decided that the original detention was void, and that unless a woman was lawfully under care and treatment in an institution or certified house or approved home or out on licence therefrom no offence against s. 56 was committed by someone who had carnal knowledge of her.

Lord Tucker, with whom Lord Reid agreed, said in his judgment that when the Crown proved that a girl was detained as an inmate in one of the specified institutions and was under care or treatment as a defective, or if she was shown by production of the licence to be out on licence from such an institution, that was prima facie proof that she was a defective lawfully under care and treatment as such. It was not for the Crown to prove in all cases under s. 56 by medical evidence before the jury that the girl came within one or other of the categories of mental defective specified in s. 1. That was to be presumed, but, if it was shown by the production of documents in evidence that the detention was on the face of those documents illegal, the prosecution must fail. It was therefore proper that the prosecution should have the relevant orders or other documents on which the detention was based in court and available for inspection by the defence so that in a proper case and subject to questions of admissibility the presumption of legality might be rebutted.

Lord Somervell said that he was not satisfied, as had been contended before the House, that the Secretary of State's order detaining the woman was not void but only voidable. It was conceded that even if it was only voidable the Court had material on which if challenged for example by *habeas corpus* the order would have been quashed. He was not satisfied that whether or not a man was to go to prison should depend on whether the order was void or voidable.

Lord Denning said that, if the Secretary of State had had no jurisdiction to make the detention order, the order would have been void. Here it appeared that he had acted with jurisdiction but erroneously, so that his order was only voidable and was to be regarded as good until set aside. He thought that even if the original erroneous order had been set aside the continuation orders would remain good. In view, however, of the course of proceedings in the Court of Criminal Appeal it would not be fair to restore the conviction.

Viscount Simonds, dissenting, said that, while the House was traditionally jealous of the liberty of the subject, this consideration was irrelevant here. This man's liberty was not at stake unless a man was to be at liberty to have carnal knowledge of any woman who was under treatment in an institution on the chance that a defect might be found in the detention order.

Accordingly their Lordships, "the voices of ultimate infallibility," dismissed the Crown's appeal by a majority of 4 to 1, and Head stays free. The Attorney-General revealed in the course of the hearing that the woman was now happily married.

[1] *The Times*, March 7.
[2] See *British Medical Journal*, November 23, p. 1247.

PSYCHIATRIST'S EVIDENCE

USE OF ANAESTHETIC DRUG

[FROM OUR LEGAL CORRESPONDENT]

On February 12 Police Constable Magness pleaded guilty before the Worthing justices to stealing a vacuum flask and three powder compact refills worth together £1 4s., and asked for a previous theft of four lipsticks worth 19s. 4d. to be taken into consideration. He was sentenced to three months' imprisonment.

In support of Magness's solicitors' plea in mitigation there was called Dr. Alexander Watt, psychiatrist, of The Acre, Boundary Road, Worthing, who handed a written report to the justices. He said that he had been unable to get the information he required from Magness by interrogation, and had used a slow injection of a mildly anaesthetic drug which had the effect of altering an individual's normal tendencies and making him talk more freely and describe things he would not otherwise recollect. Dr. Watt described what Magness had told him, and said he was satisfied that Magness was subject to recurring states of altered consciousness, which were the more likely to occur at night, and that he could have committed the offences during such states. He was mentally ill, and in a greatly disturbed emotional state.

It is to be observed that Dr. Watt's use of an anaesthetic drug to help to elicit the facts necessary for his diagnosis would require his patient's consent. To use such an aid without consent would be in law an assault. The fact that Dr. Watt was giving evidence for his patient in support of a plea in mitigation of penalty of course presupposes his patient's consent to a revelation to the court of what emerged in the course of his use of the drug. Without his patient's consent a doctor would not be justified in going into the witness-box voluntarily to reveal what had passed between himself and his patient in consultation. If, however, a doctor is subpoenaed to give evidence or has been called to give evidence and is under cross-examination, he cannot legally refuse to answer questions about what he has learnt in consultation. He cannot as a matter of law treat the secrets of the consultation as privileged from disclosure in the witness-box, any more than the Roman Catholic priest can as a matter of law claim privilege for the secrets of the confessional. As a matter of law professional privilege from disclosure is restricted to what has passed between a man and his lawyers.

[1] *Worthing Herald*, February 14.

Medical Notes in Parliament

HEALTH SERVICE ECONOMICS

The second reading of the National Health Service Contributions Bill, on March 5, was used by the Minister of Health as the occasion for an analysis of the economics of the Service, the trend and pattern of costs, and the value received.

Total cost had risen from £452m. in 1949–50, the first complete year, to £740m., an increase of £288m. Adjusting current costs to 1949–50 prices showed an increase in real terms of £80m. With some marginal adjustments for the increase in population, old people, and other factors, the measure of the inflationary increase over the period was about £200m.

The bulk of this inflationary increase was not due to the Health Service itself. It was not the prodigal habits of the Service which were forcing the inflationary pace. The increase was primarily the reflection of the inflationary tendencies in the economy as a whole. The cold, hard fact remained, however, that the cost, whatever its cause and composition, had to be met. The Health Service contributor got good value for his money, by any test. In real money terms he got a service increased in value by £80m. and by £35m. in Exchequer money. In services rendered: there had been a steady and gratifying increase in the number of new hospitals and extensions; bed occupancy had increased from 453,000 in 1950 to 478,000 in 1956. The number of doctors in general practice was just under 20,500 in 1951, and just under 22,500 in 1956; and the number of patients per doctor had fallen from about 2,500 to 2,272. The same applied to dentistry—treatments had increased from about 9½m. in 1953 to 12m. in 1956; and to sight tests, which had risen from 4¼m. in 1951 to 5¼m. in 1956. Visits by home nurses had increased from 22,600,000 to 27,600,000 over the same period. On that evidence, the case for increased efficiency and production and increased value to the consumer was clearly proved.

Breakdown of Expenditure

That did not dispose of the question whether unhurtful economies could be found in the Service. The main elements in the cost, on the 1958–9 estimates, were—hospital running costs, £399m. (just under 54% of the total cost); hospital capital cost £23m. (about 3%); general medical services, £72m. (about 10%); pharmaceutical services £74m. (10%); dental services £51m. (about 7%); local authority services £65m. (about 9%). Hospital running costs, which amounted to more than half the total, were mainly composed of wages and the cost of commercial commodities, which meant that the inflationary element was mainly a reflection of the general inflationary tendency. To ensure the greatest possible efficiency in administration the technique of organization and methods had been instituted in the hospital service. Started in September, 1954, with an experimental unit recruited from the Treasury, by last September it had completed 78 assignments covering a large number of aspects of hospital work, and had nearly completed eight comparative studies of important common procedures or services. This experience had shown that application of techniques of investigation used in business and industry could produce valuable results in the hospital service, and he was considering the best way to establish organization and methods procedure as a permanent and integral part of the Service.

Drug Bill

Another possibility of economy was the drug bill, about which there was some doubt and perhaps disquiet. The estimated cost of the pharmaceutical drug bill for 1958–9 was £74m.—10% of the cost of the Service, and more than twice the cost in the initial year. (A further £12m. or £13m. was involved in the hospital drug bill.) There were two causes for the increase—the general rise in costs and the introduction of new drugs—such as the antibiotics and cortisone. Various measures had been taken to confine the bill to its lowest reasonable cost.

Doctors had a statutory right to prescribe the drugs they thought necessary for their patients, but to give them guidance in discharging their duty economically they were issued the *National Formulary*, comparative price lists, and *Prescribers' Notes*. To restrain manufacturers' prices, an agreement was made in 1957 for a trial period of three years. The scheme covered most proprietary drugs, and its operation would be carefully studied. The Hinchliffe Committee, set up last summer to investigate the factors in the cost of prescriptions, had been asked to make interim recommendations if it could usefully do so.

The search for economies that could be achieved without detriment to the patient and the Service was unceasing, but the analysis showed that the scope for such economy was not nearly as large as some people imagined. The total cost had increased in spite of all practical economies, and they could not guarantee a stabilization at the present figure. The main element in this steady and hitherto apparently uncontrollable rise was a reflection of the general inflationary tendency. The principle of unlimited Exchequer liability was clearly inconsistent with a disinflationary policy.

Turning aside for a time to answer political criticism of the increased charge as a regressive tax bearing disproportionately heavily on the lower-paid workers—which had been the substance of the previous week's debate on the Ways and Means resolution for this Bill—the Minister claimed that these increases were tiny percentages of income, as indeed was the whole incidence of the Health Service contribution. Advocacy of the Bill as right in current circumstances, but not an end in itself, brought him back to the larger issue and the prospect of a sounder financial future for the Health Service.

The first impact of the "increased productivity" of the Service had been on overtaking arrears of treatment rather than reducing total cost. Something of what could be done had been shown by the dramatic reduction in the calls on the hospital service—for example, in tuberculosis. In future this pattern might be seen reflected in other diseases. Proper home treatment for the old people and the mentally ill could also show a reduced burden on hospitals, and a real saving in money and resources. But the Health Service could have a sound financial basis only by ridding the whole economy of its inflationary virus.

Bill a "Panic Measure"

Dr. EDITH SUMMERSKILL (Warrington, Lab.) described the Minister's survey as superficial, but she did not blame him because successive Ministers had been incapable of grasping during their short period of office the ramifications and problems of the Health Service. The policy of casting about every few months to provide a comparatively small sum showed administrative ineptitude. She did not oppose the provision of a further £32m. for the Service. Indeed, it would be very difficult to reduce the cost of the Service in the future, and there was every probability that it would be increased. But the method was indefensible, and a panic measure. She renewed her attack on the high-powered salesmanship of the drug houses, and went on to question hospital costs, and to suggest the encouragement of group practices, which could reduce the number of out-patients, extension of home nursing facilities, and investigation of the cost of part-time as opposed to full-time consultants. What was needed was a rethinking and reviewing of the Service, not a Bill hurriedly designed to see the Government over a difficult period.

Hospitals Starved of Capital

Mr. R. H. TURTON, a former Minister of Health, found a weakness in the social security schemes in that so high a proportion of the expenditure—58% according to I.L.O.

figures—came from the central Government. There was no way of keeping the price factor in the minds of those using or administering the Service. It hampered capital development. Before the war the relationship of capital expenditure to current expenditure on hospitals was 19.6%. After the war it dropped to 4%. Now it was 6%. Hospital boards and local authorities had been starved of capital expenditure. He believed that by spending more in this way they could save money on current expenditure in later years. On a flat-rate contribution there was a limit to which contributions could be raised. He thought there should be examination by a Royal Commission of the financing of social security. If there was to be a graded insurance contribution it should be merged with the pay-as-you-earn scheme. He regretted that his contribution was not earmarked for a special part of the health expenditure, such as the general medical and pharmaceutical services, because then all would realize how the insurance was linked with the visit to the doctor and getting the drugs.

Dr. DONALD JOHNSON (Carlisle, Con.), speaking of the changing pattern of disease, sought assurance that the Minister as well as being familiar with it was taking action quickly enough to make the necessary economies as it was taking place. The separation of hospitals from the local authorities as well as from the general practitioners had created a load on the hospital system which probably had been the most prominent feature of the past 10 years' development. The hospitals often increased the load by telling out-patients to keep attending, when they could well go back to their own doctors. On the vexed question of drugs, he said that the newer drugs had been used not only for serious illness but for a variety of minor complaints capable of much simpler treatment. The result had been the creation of drug-resistant germs, involving the development of still further antibiotics at still greater expense—producing a snowball of expense and at the same time an indifferent form of medical practice.

Dr. Charles Hill Winds Up

Dr. CHARLES HILL, Chancellor of the Duchy of Lancaster, deprecated undue insistence on the provision of a fixed proportion of the national product for the Health Service. The day might be reached when the cost of the Service, because of its success, would represent a smaller proportion without being inferior; or because of a fall in the national product there might be what looked like a percentage rise for the Health Service without there being a real rise. From 1950 to 1954 there was a declining proportion of the national production, and from 1954 to 1956 there had been a modest increase in the proportion. He declined to follow Dr. Summerskill into the details of the drug bill, except for the general observation that there was a widespread passion for medicine in this country. On the future of the part-time consultant service, he said that was one of the matters on which the Royal Commission was taking evidence, and he would offer only three reflections. If it were decided to convert all part-time consultants into whole-time consultants, that would raise the cost. If they took the number of whole-time consultants who were needed for the hospital job they would have to sack some consultants and deprive them of their hospital experience. Even if they did that, on a rough calculation the economy would be between £1m. and £1½m., out of a total bill for the consultant services of over £20m.

The Bill was given a second reading by 308 votes to 252.

"YOUR LIFE IN THEIR HANDS"

When the House of Commons met on March 7, Mr. ERNEST MARPLES, the Postmaster-General, made the following statement.

"At Question Time on February 26 I referred to the B.B.C.'s consultation with medical authorities about the programme *Your Life in Their Hands*. This seems to have given rise to some misunderstanding. I would like to clear up this misunderstanding.

"I am informed by the B.B.C. that the Corporation had had wide and detailed discussions with medical, surgical, and nursing staffs both on the subject matter of the programmes, as well as their method of presentation. Before the first broadcast, the B.B.C. held a conference. At this conference, representatives of the Royal College of Surgeons, the Royal College of Physicians, and members of the College of General Practitioners were present, together with other interested medical men and representatives of the medical press. Nothing occurred as a result of this informal consultation to suggest to the B.B.C. that its programmes would meet with opposition from the bodies concerned, or that the Corporation ought not to proceed with its plans. Correspondence after the first broadcast from members of the medical profession and others confirmed the B.B.C. in this view.

"I regret that the information I previously passed on to the House implied a more formal degree of consultation between the B.B.C. and the medical bodies mentioned, as well as a formal expression of their subsequent appreciation of the programme. This appears to have arisen from a misunderstanding between my department and the Corporation. I am glad to have had this opportunity of explaining more fully the degree of consultation between the B.B.C. and the medical bodies concerned before the programme began."

Mr. W. GLENVIL HALL, the senior Labour ex-minister present, said that the Opposition accepted whole-heartedly the statement which Mr. Marples had made. It was in the best tradition of the House that when ambiguity or misstatement was made the Minister or any other Member should take the earliest opportunity of putting the matter right.

Law on Suicide

The following motion, supported by some thirty members from both sides of the House, has been put down by Mr. KENNETH ROBINSON (St. Pancras, North, Lab.):

That this House is of opinion that the existing law of England relating to suicide has no deterrent effect, is capricious in its incidence and can no longer be regarded as reflecting the attitude of society; and considers that suicide and attempted suicide should now be removed from the category of criminal offences.

Russian Vaccine for Multiple Sclerosis*

Mr. JOHN MCKAY (Wallsend, Lab.) and Mr. F. BROCKWAY (Eton and Slough, Lab.) asked the Minister of Health on February 24 to arrange for the importation of the Russian vaccine for the treatment of multiple sclerosis, and in particular to permit the importation of special supplies for two named persons. Mr. WALKER-SMITH told them he was advised that the evidence at present available was not sufficient to enable an opinion to be given on the efficacy or safety of this vaccine. In these circumstances it would be quite wrong for sufferers to be encouraged to build their hopes on it, and no arrangement for its general importation could be justified. He was, however, prepared to advise the release by the Customs and Excise of small quantities obtained for individual treatment on the advice of a patient's medical practitioner. He added, in further replies to Dr. EDITH SUMMERSKILL and others, that private importation in the circumstances he had mentioned was not prohibited. No application for a licence for commercial importation had been made. His medical advisers were naturally inquiring into the claims made for this vaccine. He was advised that one of the originators of the vaccine claimed no more than that it helped about one-third of the patients treated. The Ministry would certainly seek all the information it could, and do all the research it could.

Prescriptions Not Used

The MINISTER OF HEALTH told MRS. LENA JEGER (Holborn and St. Pancras South, Lab.) on March 3 that he had no evidence that some patients, on grounds of expense, were

*See *British Medical Journal*, January 4, p. 7, for a report from the department of microbiology, Queen's University, Belfast, of an investigation of this vaccine—"the vaccine of Margoulis and Choubladze."

collecting fewer than the total number of items on their prescription forms. Mrs. Jeger said that it was happening frequently. There were chemists in the London area who found it happening about once a week. They were being put in an impossible position, and were sending prescription forms to the executive council marked "Not Supplied." Why did the Minister not know about these things? Mr. WALKER-SMITH said that Ministers and Departments were normally quickly told when things were thought to have being going wrong. He had not received any evidence, by letter or otherwise, to this effect. If Mrs. Jeger had any evidence he would consider it with the greatest care. Dr. EDITH SUMMERSKILL asked if anyone in the Department had asked chemists in the London area whether this was so or not. Mr. WALKER-SMITH: I do not think it would be appropriate to carry out a sort of roving inquiry unless they started with the firm base of some evidence supplied by somebody.

Senior Registrars

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Minister of Health, on March 10, when he expected to meet the Joint Consultants Committee to discuss the senior registrar problem. Mr. D. WALKER-SMITH: Tuesday, March 25.

Mr. ROBINSON asked the Minister if he would, if necessary, impose his own solution. Mr. WALKER-SMITH said he would not like to go into discussions of that sort on any assumption other than that reason would prevail, and that they would get a proper and reasonable solution harmoniously in agreement together.

Mr. J. CRONIN (Loughborough, Lab.) asked the Minister why he had made it a condition for relieving the difficulties of senior registrars that the medical profession should agree to the setting up of a number of new special posts, not previously provided for in the Health Service, in which the duties were similar to those of consultants, whereas the salary and status were substantially inferior to those of consultants. Mr. WALKER-SMITH: No such condition has been made. Mr. CRONIN said the medical profession would be glad to hear that. Did the Minister appreciate the awkwardness that arose when his representatives said one thing and he said another? Mr. WALKER-SMITH: I cannot accept that statement. My representatives have not said anything contrary to what I have said in the House. I ask Mr. Cronin to believe that we really would get on better if we were able to have these discussions with the committee, rather than that he should interpret on a basis of hearsay what he thinks is going on.

Mr. CRONIN asked on how many occasions representatives of the department had had meetings with the Joint Consultants Committee during the last two years to discuss the difficulties of senior registrars in the Health Service; and what had been the obstacles to reaching agreement. Mr. WALKER-SMITH: There have been 10 meetings at which the general question of hospital medical staffing, including the senior registrar aspect, has been discussed. As I am to meet the Joint Committee I would prefer not to make any statement on the discussions at this stage.

Training of Psychiatrists

Mr. KENNETH ROBINSON asked the Minister if he would initiate discussions with the teaching hospitals, the Royal Colleges, and the Institute of Psychiatry on the urgent need to train more psychiatrists. Mr. WALKER-SMITH replied that the question whether there was a need for more training posts in psychiatry and other specialties would shortly be discussed with representatives of the profession. Mr. ROBINSON said he was glad to hear that answer. The key to the serious shortage of psychiatrists lay in the teaching hospitals. Some initiative had to be taken, probably by the Minister and the department, to get over the highly conservative medical curriculum. Mr. WALKER-SMITH said the intake of senior registrars graded in psychiatry was actually larger than in any other specialty, and had recently been further increased. There had also been a substantial increase in the number of registrars, to the extent of 39%, between 1953 and 1956.

Radioactivity of Tobacco

Mr. F. BESWICK (Uxbridge, Lab.) asked the Minister of Health, as representing the Lord President of the Council, what research by the Medical Research Council had been done into the radioactive properties of the tobacco plant and tobacco ash, and with what result. Sir M. STODDART-SCOTT (Ripon, Con.) had a similar question. Mr. WALKER-SMITH said that measurements of the radioactive content of tobacco, tobacco ash, and tobacco smoke had been carried out under the auspices of the Medical Research Council. There was no evidence that the radioactive content of the tobacco plant was in any significant manner different from that in other forms of vegetable life. Very little radioactivity could be detected in tobacco smoke, since the greater part of the radioactivity in the plant remained in the ash. The Lord President was advised that the dose of radiation to the lungs from this source, even in heavy smokers, was so small that it was unlikely to be a factor of any importance in the causation of cancer of the lung. Mr. BESWICK said that a certain amount of work had been done to disprove some of the conclusions that had been drawn. Government research departments had stated that the radioactivity of the tobacco plant was higher than that of any other vegetation. It absorbed more readily the chemical radioactive material in modern fertilizers. Although this was not sufficient itself to cause lung cancer, it was superimposed on the background of other radioactive properties in smog and other conditions of modern life. Was it not worth while going into the matter again? Mr. WALKER-SMITH said that neither complacency nor contradiction was involved. Measurements of the radioactivity in various forms of tobacco were taken under M.R.C. auspices by research workers in the department of medical physics at Leeds University in 1953. The results had been confirmed by other research groups, including Professor Mayneord's group at the Institute of Cancer Research.

Dismissed Surgeon

Mr. CRONIN asked the Minister of Health if he would reinstate Mr. Alexander Howard Barber, a consultant surgeon, who was dismissed from the National Health Service on April 30, 1952, having regard to the circumstances that he was recently awarded in the High Court £7,437 damages against the Manchester Regional Hospital Board for wrongful dismissal and granted a declaration that the Minister had acted wrongfully and in breach of statutory duty in not hearing his appeal against the dismissal. Mr. WALKER-SMITH: I have no power to do so.

Universities and Colleges

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following candidates have been approved at the examinations indicated:

M.D.—A. D. H. Browne.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part II*: F. King, N. A. J. Mullen.

UNIVERSITY OF LONDON

Dr. A. B. Wayte has been recognized as a teacher of radiotherapy at Guy's Hospital Medical School; Dr. David Sutton as a teacher of radiology at the Institute of Neurology; and Dr. Hans Kalmus as a teacher of biology at University College.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examinations indicated:

FINAL M.B., CH.B.—M. G. Addy, A. A. Codd, J. C. G. Cole, J. S. Edmondson, R. R. Gibbins, D. H. Howton, O. Lartey, J. G. Meadows, K. J. Roper, G. A. Russell, R. F. Weeks, R. C. Williams. *In Group I, completing the examination*: C. N. Bruton. *In Group II only*: J. E. Aslett, Yvonne E. J. Marot, V. P. Nagpal, M. P. Patel. *In Section I*: J. E. Aslett, M. B. Clark, Joan D. Clay, P. T. Gardner, G. D. Henley, Daphne M. O'Connor, A. H. Ogden, P. C. Power, Anne P. Simon.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At the quarterly comitia of the College held on January 30, with the President, Dr. Robert Platt, in the chair, Dr. G. E. S. Ward was re-elected College representative on the Council of the Queen's Institute of District Nursing and Professor A. A. Moncrieff on the Central Midwives Board. Dr. Donald Hunter and Professor G. M. Wilson were elected College representatives on the Joint Formulary Committee; Dr. E. R. Boland, Dr. J. B. Harman, and Dr. T. C. Hunt on the Central Medical Recruitment Committee for 1958–9; and Sir John Charles to the Health Congress of the Royal Society of Health to be held at Eastbourne from April 28 to May 2, 1958.

Licences

Licences to practise were conferred upon the following 106 candidates who have passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and who have complied with the by-laws of the College.

Shirley A. P. Abell, J. R. Allan, D. L. Aspinall, K. A. Barlow, R. D. S. Barnes, A. M. Barnie-Adshead, Elizabeth S. Bates, Mary E. Braithwaite, D. J. Burgess, J. F. Cam, Jean A. Cam, A. R. O. Chinery, W. R. Chisholm-Batten, A. Chynoweth, M. Ll. Clark, C. J. Clemenson, G. B. Cornford, D. Cowap, A. Cox, Sheila M. Creegan, Jane M. Critchley, C. W. Currivan, G. A. W. Dove, J. K. Duff, Una M. Dugan, T. F. Dunham, M. K. Dunstan, P. Eckhart, H. J. Edwards, R. W. Elsdon-Dew, H. C. Evans, P. A. Evans, D. R. Firth, Judith A. G. Fletcher, Mehroo Forbes, C. J. Ford, G. Hamlet, L. D. Heap, J. Hellewell, L. W. H. Hide, D. I. R. Higton, Jillian M. Home, B. Howarth, Rosemary J. Huntley, P. W. James, B. F. Johnson, J. M. Ll. Jones, J. E. Keithley, Mary B. Kelly, B. S. Kennett, J. R. Lane, Patricia A. Last, J. M. Laurent, G. I. M. McLellan, Jean L. McNair, S. A. F. O. McNamara, C. K. Manuel, B. S. Mather, H. Meindok, Lilianna Melzak, J. C. Merrington, P. V. Meswani, A. B. J. Miller-Williams, Gillian R. Montague, D. T. Morris, P. M. Morris, V. P. Nagpal, T. W. Otway, K. M. Patel, G. R. Peachey, B. M. Phillips, Sheila P. I. C. Phillips, Alina T. Piesowicz, H. D. W. Plowright, Betty L. Priestley, A. K. Ritchie, J. Rivilis, P. A. Robson, B. A. Ross, V. Rudralingam, R. M. I. Shacksnovis, Nina Shotts, J. O. Sibthorpe, N. A. Simmons, K. M. Simpson, D. S. Smith, E. O. Sofowora, J. K. Stonham, Gillian Strube, R. H. Sun, P. T. H. Tay, Diana Thornton, R. E. Tonge, D. G. Tranter, J. V. Traater, Rita C. Travers, Pamela Walton, P. J. Whitfield, D. M. L. Williams, G. Williams, Julia M. Winter, P. J. Wise, B. J. P. Wright, J. E. C. Wright, R. J. Young, I. I. Zayid.

Diplomas

The following diplomas were granted jointly with the Royal College of Surgeons of England:

DIPLOMA IN INDUSTRIAL HEALTH.—H. D. R. Zscherpel.
DIPLOMA IN MEDICAL RADIOTHERAPY.—R. Diaz Perches.

Diplomas in Laryngology and Otology, in Anaesthetics, in Medical Radiodiagnosis, in Psychological Medicine, in Tropical Medicine and Hygiene, in Pathology, in Public Health, and in Child Health were granted jointly with the Royal College of Surgeons of England to the successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England held on January 9.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on January 9, with Sir James Paterson Ross, President, in the chair, the deaths of Sir Thomas Dunhill (Honorary Fellow) and Viscount Waverley (Hunterian Trustee) were reported and noted with deep regret.

A diploma of Fellowship was granted to A. B. Cassie, and a diploma of Membership to V. P. Nagpal.

The following diplomas were granted jointly with the Royal College of Physicians of London:

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—P. Abbey, R. Ahmad, Z. H. Alvi, J. Bihari, T. Cartmill, R. R. A. Coles, B. R. Das, M. J. D'Cruz, J. L. Godden, J. Hali-Jones, M. Horowitz, Y. P. Kapur, G. M. Khan, F. W. Kwok, I. Narain, N. B. Parvathiah, J. Potter, L. N. Prasad, R. Prasad, I. P. C. Robertson, D. S. Sardana.

DIPLOMA IN ANAESTHETICS.—F. D. Adrianvala, Eleanor K. Althorp, Edna W. Anthony, N. K. Ashurst, Roma M. Bedford, A. Berry, Jane I. K. Binnie, H. L. Blake, Margaret A. E. Boyce, J. H. Breed, R. A. Butler, P. H. Byles, Joan M. Byrne, P. S. Chau, J. M. Clark, R. J. Clark, W. H. Cochrane, G. F. Conway, S. K. Coombes, H. B. Coulter, Bridget M. Cowley, H. J. L. Craig, J. P. Czyniewski, M. A. de Valero Wills, B. J. Dolan, R. R. Evans, A. D. J. Farquharson, M. E. Fielding, G. Flowers, H. J. Freedman, B. I. Gupta, V. G. Gurjar, C. Gyaw, R. W. Hall, D. D. Hart, D. F. Hogan, Margaret C. Holderness, W. G. Holland, Ann Horsburgh, T. H. Howells, Ayesha S. Ishrat Husain, M. O. N. Iyengar, T. E. Jones, V. R. Jones, Kathleen E. Kennedy, J. C. Kennedy Smith, J. D. Kinnell, R. J. Knight, H. P. Lacey, R. G. Lacey, A. Lagowski, G. L. F. Lau, P. D. Lawler, J. L. Layng, Phyllis L. Liddle, G. J. M. Lincoln, J. V. McCooey, P. W. McCormick, S. W. McGowan, N. N. Madan, R. E. W. Manley, R. R. Manning, Maung U. Win, T. W. P. Millar, J. S. Miller, Mary H. Miller, D. R. Morgan, Ada C. Morrison, Joyce Newman, B. A. Nixon, K. Parohoo, T. F. J. Parker, A. S. Paton, P. A. P. Pompa, Diana Ratcliffe, D. D. G. Simpson, C. Singh, H. Somowitz, J. A. Stainton-Ellis, K. D. Stephenson, C. R. Sulochana, N. S. Thomas, J. S. Toner, Patricia A. Topham, S. R. Umrigar, R. D. Unkles, S. Vankieti, F. H. Walter, Elizabeth M. B. Watson, A. I. Weinreich, J. M. S. Whiting, D. C. M. Wilcox, P. F. Willis, J. E. York, Freda Young.

DIPLOMA IN MEDICAL RADIO-DIAGNOSIS.—D. A. Alderson, K. Ashcroft, K. Aung, W. R. Barrow, D. C. Bernstein, M. P. Bhalla, S. Bissylass, H. J. Bloch, R. Cable, D. F. Cantwell, G. Cohen, I. D. Davies, M. L. Dyson, R. F. Fouche, J. Fraser, R. W. Galloway, J. J. Gately, K. Grainger, I. Isherwood, N. Joffe, Brigid Keane, J. T. Lamb, J. Lees, J. J. D. Lobo, A. B. McGrigor, M. R. H. Mahmood, R. C. Michell, N. L. Mills, I. Movsas, N. D. C. O'Connell, Irmgard Patton, J. J. Prior, K. D. Reddy, P. Reichman, B. Ridgway, J. H. Rustage, A. Sardar, H. M. Saxton, S. N. Sender, M. P. Shannon, E. Sheville, M. J. Strachan, H. M. Strathern, D. F. Street, G. Sullivan, S. N. B. Talwatte, S. Taneja, R. P. Vass, P. Ward, W. L. Wong.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—G. H. Armitage, Grace Bainbridge, A. H. Borowitz, A. M. Bradfield, S. W. G. Caseley, M. R. Chaudhry, A. B. Cooper, F. H. Corbitt, J. McK. Davie, R. N. Davis, J. Erulkar, G. W. Fenton, A. Gage, M. E. Grant, I. Hadfield, L. Harris, P. Hays, G. A. Heasman, Mary K. P. Henderson, W. Leggat, K. Loucas, N. C. Low, S. M. Macentee, N. K. Macrae-Gibson, W. K. Marshall, Pamela G. L. W. Mason, W. J. Nicholson, V. R. Ntsekhe, P. M. J. O'Brien, J. R. Palmer, Barbara Petrovskaia, A. Pick, E. W. Poole, J. H. Price, J. R. Roy, Barbara J. Salisbury, G. H. Scott, J. C. Scott, K. Singh, W. B. Spry, J. S. Stead, A. A. Sugerman, S. S. Syalee, W. D. Wilson, W. Wolfen.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—H. F. McElligott, U. Sahay, T. Tharmaratnam.

DIPLOMA IN PATHOLOGY.—B. B. Beeson, P. W. J. Bosman, S. M. Deoras, G. Garrett, Barbara E. Grahame, I. J. Hunter, F. Kurrein, C. J. McDonald, J. Ward.

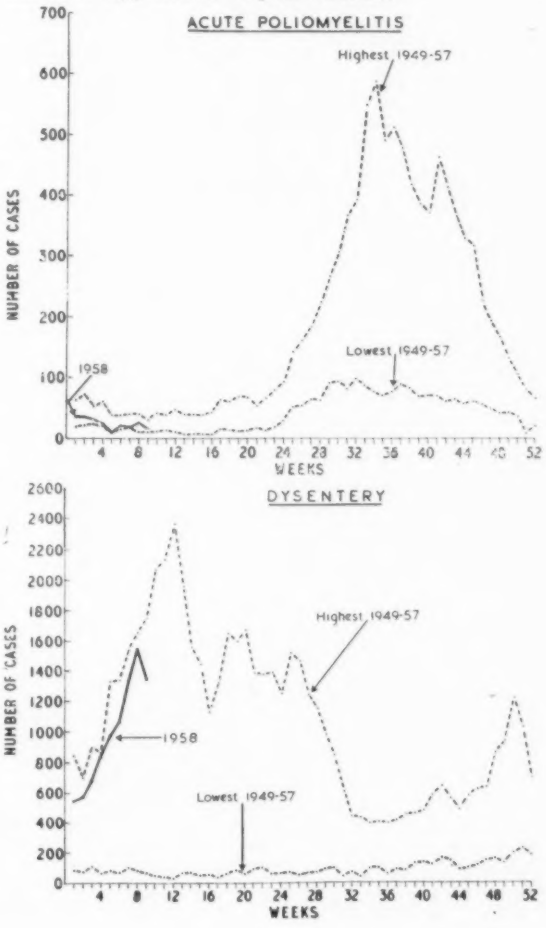
DIPLOMA IN PUBLIC HEALTH.—Mary M. M. Boyd, M. J. Catton, M. L. Graeme, B. Hussain, P. V. Krishnamurti, C. L. Milburn, S. K. Sen, Tin U, E. J. Wright.

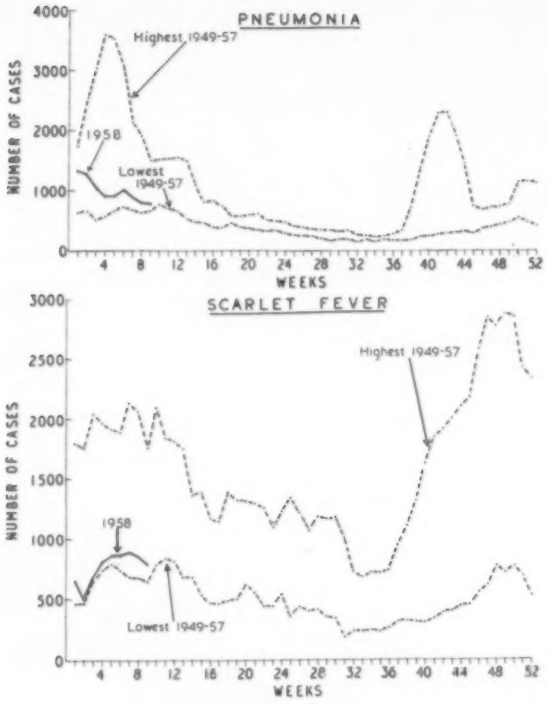
DIPLOMA IN CHILD HEALTH.—D. J. Clark.

Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Week Ending March 1

Infectious diseases were less prevalent in England and Wales during the week ending March 1. The decreases in the number of notifications included 235 for measles, from 4,618 to 4,383, 212 for dysentery, from 1,545 to 1,333, 121 for whooping-cough, from 645 to 524, 64 for food-poisoning, from 188 to 124, 56 for scarlet fever, from 853 to 797, and 20 for acute pneumonia, from 793 to 773.

The largest falls in the incidence of measles were 106 in Hertfordshire, from 205 to 99, 87 in Derbyshire, from 248 to 161, 85 in Glamorganshire, from 516 to 431, and 84 in Lancashire, from 422 to 338; the largest rises were 120 in Hampshire, from 344 to 464 (Fareham U.D. 129, Portsmouth C.B. 107, Southampton C.B. 84), and 103 in Dorsetshire, from 44 to 147 (Poole M.B. 37, Wareham and Purbeck R.D. 37, Wareham M.B. 33). The largest fall in the number of notifications of whooping-cough was 40 in Yorkshire West Riding, from 72 to 32. The largest variation in the trends of scarlet fever was a decline of 23 in Staffordshire, from 65 to 42. 3 cases of diphtheria were notified, being 3 fewer than in the preceding week. The notifications of acute poliomyelitis numbered 15, and these were 5 fewer for paralytic and for non-paralytic cases than in the preceding week. The only area with more than 1 case was Hampshire, Petersfield R.D., where 2 cases were notified.

The chief centres of dysentery were Lancashire 444 (Oldham C.B. 125, Liverpool C.B. 67, Whiston R.D. 64, Manchester C.B. 31, St. Helens C.B. 31, Middleton M.B. 23, Chadderton U.D. 17, Rochdale C.B. 13, Heywood M.B. 11, Failsworth U.D. 10), Yorkshire West Riding 245 (Sheffield C.B. 106, Hemsworth R.D. 32, Leeds C.B. 21, Barnsley C.B. 20, Saddleworth U.D. 18), London 159 (Fulham 36, Islington 16, Stoke Newington 16, Kensington 15, Finsbury 11, Hackney 10, Southwark 10), Caernarvonshire 81 (Pwllheli M.B. 37, Bangor M.B. 16, Lleyn R.D. 11), Cheshire 71 (Wallasey C.B. 38, Sale M.B. 14), Surrey 55 (Kingston-upon-Thames M.B. 36, Richmond M.B. 10), Middlesex 44 (Willesden M.B. 15, Ealing M.B. 11), Durham 34 (Whickham U.D. 14), and Nottinghamshire 29 (Basford R.D. 16, Nottingham C.B. 12).

A large outbreak of paratyphoid B is reported from Tipperary. In the week ending February 22, 63 cases were notified, and 30 in the week ending March 1.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 22** (No. 8) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	1	4	0	1	2	0	2	0	4
Dysentery	1,545	192	192	30	1	1,296	93	414	15	5
Encephalitis, acute	0	0		0		1	0		0	
Enteric fever:										
Typhoid	2	0	0	0	2	1	1	2	0	1
Paratyphoid	0	0	0	0	72 (B)	8	1	1 (B)	0	
Food-poisoning	188	17	20	0		139	16	15	1	
Infective enteritis or diarrhoea under 2 years				11	13				10	23
Measles *	4,618	153	105	26	30	21,317	1945	500	477	346
Meningococcal infection	35	0	11	0		26	1	10	1	1
Ophthalmia neonatorum	26	1	14	0		27	1	8	0	1
Pneumonia †	793	54	338	11	43	625	45	241	16	2
Poliomyelitis, acute:										
Paralytic	15	2	0	2	2	30	0	1	0	5
Non-paralytic	10	0				9	2			
Puerperal fever §	224	31	6	0		237	40	10	1	
Scarlet fever	853	53	82	23	13	890	62	87	30	40
Tuberculosis:										
Respiratory	537	69	96	20		672	88	116	16	
Non-respiratory	58	3	10	1		86	4	12	5	
Whooping-cough	645	31	49	4	14	3,190	158	375	71	57

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	3	1		0			0		0	
Encephalitis, acute		0					0			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	3	1	0		0	0	0	0
Influenza	100	4	3	0	2		0	1	1	0
Measles		0	0	0	0		1	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	819	67	29	17	10		42	31	14	8
Poliomyelitis, acute	1	1		0	0		0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	88	12	15	2	5		5	8	1	6
Non-respiratory		1	0	0	3		1	2	0	0
Whooping-cough	1	0	0	0	0		0	1	1	0
Deaths 0–1 year	388	34	33	5	18		25	34	5	10
Deaths (excluding stillbirths)	11,524	953	718	155	241		845	647	128	208
LIVE BIRTHS	14,725	1227	1029	229	343		1162	989	205	364
STILLBIRTHS	332	31	25				25	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

National Association for Mental Health.—Mr. R. A. BUTLER, the Home Secretary, announced on March 6 that the Government would introduce legislation to give effect to many of the proposals of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency. This would not be during the present parliamentary session, but might be in the next. Mr. Butler was speaking at the opening of the two-day annual conference of the National Association for Mental Health, which was held at Church House, Westminster, on March 6 and 7. The conference was opened by the DUCHESS OF KENT, and had as its subject the implications for local authorities and the general public of the Royal Commission's report. Mr. BUTLER pointed out that one of the major problems would be the translation of recommendations made by the Commission into legal form. It was essential that satisfactory legal definitions should be found for the various types of mentally ill persons who might be liable to compulsory detention.

The Medical Society of London.—The 178th anniversary dinner of the Medical Society of London was held in the Royal College of Surgeons on March 6. In proposing the toast of the Society, Lord MOUNTBATTEN, referring to the foundation of the Society in 1773, said that three members were then resident in the North American colonies. Looking into the history of its founder, Lettsom, he calculated that Lettsom in one year earned the equivalent of £300,000 in terms of the value of money to-day. Lord Mountbatten went on to express his gratitude to the medical profession for their great contribution to the war in the Burma campaign. To begin with, for every casualty there, there were 120 men sick. In 1944, for every casualty there were 40 sick, and at the end of the war the proportion had fallen to six sick men for every casualty. In reply, the president of the Society, Sir CECIL WAKELEY, reviewed its activities during the past year. The toast of the guests was proposed by Mr. E. G. MUIR, who made everybody feel at home. In response Dr. T. F. FOX livened the proceedings with what was more an entertainment of great wit than a speech, and much appreciated by those present.

Wellcome Museum.—On March 11 there was a short ceremony at the Wellcome Museum of Medical Science, Euston Road, London, N.W.1, to mark the completion of its reorganization. The museum deals mainly with the subject of communicable disease in man, particularly as it relates to the tropics, and in this field there have been great changes in recent years. Emphasis has shifted so that diseases of the first importance when the museum opened in 1914 are no longer so, while other conditions then perhaps unknown or of relatively less importance have now come to the fore. The purpose of the present major reorganization has been to take account of these changes. For instance, virus diseases now have eight bays allotted to their illustration, whereas the space given to syphilis has been reduced to an eighth of what it used to be. Diseases are presented synoptically. A written account is illustrated and supplemented by pictures, charts, diagrams, pathological specimens, and photomicrographs. And in each bay folders containing abstracts of current literature keep the material up to date. Another help for the user of the museum is a small, well-illustrated book which describes the scope and contents of the museum. The major subjects covered are protozoal diseases, bacterial diseases, helminthic infestations, virus diseases, tropical haematology, nutrition, fungus diseases, infections due to large viruses and rickettsiae, spirochaetal diseases, and medical zoology. Last year some 10,000 doctors, nurses, medical students, and others visited the museum.

Carlsberg-Wellcome Fellowship.—Applications for the 1958–9 Carlsberg–Wellcome travelling research fellowship for a British research worker are now invited. The closing date for applications is April 30.

The directors of the Carlsberg Foundation, in Copenhagen, and the Wellcome Trustees, in London, instituted in 1957 a system of Carlsberg–Wellcome travelling research fellowships, with the object of encouraging friendly co-operation, on an exchange basis, between Danish and British research workers in any branch of the natural sciences which has a bearing upon human and animal medicine. One fellowship annually is awarded to a candidate from the United Kingdom for a year's work in Denmark and one annually to a Danish candidate for a year's work in the United Kingdom. The stipend may range from £800 to £1,200 per annum (or the equivalent sums in Danish kroner) for whole-time research. Travelling and some incidental expenses are provided in addition. It is intended that the second appointment shall be made in respect of the academic year beginning in September, 1958.

Inquiries about these Fellowships from candidates in the United Kingdom should be addressed to the scientific secretary of the Wellcome Trust, 52, Queen Anne Street, London, W.1, from whom further particulars may be obtained.

Benger Prizes for Family Doctors.—The 1957 Benger Prizes for "Original Observations in General Practice" were awarded last week at an entertaining and unusual ceremony, for the first prize winner was in the Queen's Hotel, Montreal, and the second and third prize winners were in the Connaught Rooms, London. A transatlantic "hook-up" by telephone kept the two gatherings in contact with each other for nearly one hour. Sir CLAVERING FISON opened the proceedings in London by thanking the family doctors all over the world who had responded to the challenge and entered for the prizes. Dr. JACK MACKENZIE, president of the College of General Practitioners of Canada, then presented the first prize of £250 to Dr. E. Hugh Evans, of Rockingham, Nova Scotia. After Dr. Evans, in Montreal, had briefly summarized his essay on "The Susceptible State to Viral Infections," Sir Clavering Fison presented the second prize of £150 to Dr. J. F. Burden, of Torquay, Devon, for his paper on "The Postural Density Change of Urine," and the third prize of £100 to Dr. J. J. Hobbs, of Ashington, Northumberland, for his paper on "The Administration of Pitocin for the Stimulation of Labour." Entries for this year's competition must be in the hands of the chairman of the Awards Committee, College of General Practitioners, 54, Sloane Street, London, S.W.1, by July 31, 1958.

Lecture Theatre for Royal Faculty.—The Maurice Bloch Trust is giving £20,000 to the Royal Faculty of Physicians and Surgeons of Glasgow for a new lecture hall. The hall will be built on a site behind the Faculty's present premises. The Maurice Bloch Trust is the creation of Sir MAURICE BLOCH, honorary president of the Glasgow Jewish Board of Guardians.

Royal Society of Edinburgh.—Among those whose election to the Royal Society of Edinburgh was announced on March 3 were Dr. I. R. W. LOMINSKI, senior lecturer in bacteriology, Glasgow University; Dr. ANDREW MEIKLEJOHN, senior lecturer in industrial health, Glasgow University; Dr. R. V. RAJAM, Government General Hospital, Madras; and Professor M. F. A. WOODRUFF, professor of surgical science, Edinburgh University.

Harben Medal and Smith Award.—The council of the Royal Institute of Public Health and Hygiene has awarded its triennial Harben medal to Sir HOWARD FLOREY, F.R.S., for his eminent services to the public health. The triennial Smith award to an M.O.H. recognized as having done the most noteworthy work in the discharge of his official duties has been made to Dr. C. F. WHITE, formerly M.O.H., City of London. The presentations will be made on July 10.

Sir Hans Krebs, F.R.S., Whitley professor of biochemistry at Oxford, has been awarded the gold medal of the Netherlands Society for Physics, Medical Science, and Surgery.

COMING EVENTS

Drug Action.—Symposium on "Quantitative Methods in Human Pharmacology and Therapeutics," March 24 and 25, at the Wellcome Building, Euston Road, London, N.W.1. Arranged by the Co-ordinating Committee for Symposia on Drug Action. Details from Dr. D. R. LAURENCE, University College Hospital Medical School, University Street, London, W.C.1.

Mental Health Research Fund.—The seventh annual meeting will be held on March 25 at the Royal Society of Medicine, London. The business meeting at 4 p.m. will be followed at 5 p.m. by a public meeting.

Lister Festival Dinner.—At the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, March 28, at 7.15 for 7.45 p.m. Tickets (50s. inclusive) from Mr. W. F. DAVIS at the college.

Institute of Dermatology.—Semi-permanent exhibition from March 31 to April 25, on "Moniliasis."

Association of Surgeons of Great Britain and Ireland.—Annual meeting, April 10–12, in Belfast. Details from the association, 47, Lincoln's Inn Fields, London, W.C.2.

Radiation Hazards.—Course for medical officers of health, April 10–12, at the Royal Society of Arts, 10, John Adam Street, Adelphi, W.C.2. The course has been arranged by the Services Group of the Society of Medical Officers of Health, Tavistock House South, Tavistock Square, London, W.C.1.

Refresher Course.—For general practitioners at the Southern Hospital, Dartford, Kent, on each Friday from April 11 to June 20, at 2.45 p.m. Details from Dr. J. C. HOGARTH at the hospital.

"Mental Health in the Public Health Field."—Residential course for M.O.H.s at Lupton Hall, Leeds, April 11–19. A few vacancies remain. Apply to northern secretary, National Association for Mental Health, 9, Mount Preston, Leeds, 2.

Institute of Psychiatry.—Lecture and demonstration courses for postgraduate students in psychiatry, commencing April 14, at the Maudsley Hospital, Denmark Hill, London, S.E.5. Details from the hospital.

Ophthalmological Society of the U.K.—Annual congress, April 17–19, in Cardiff. Details from the society, 47, Lincoln's Inn Fields, London, W.C.2.

Biochemical Society.—Annual general meeting, April 18 (10.45 a.m.) and 19, at University College, Gower Street, London, W.C.1. Details from Dr. C. E. DALGLIESH, Postgraduate Medical School of London, Ducane Road, London, W.12.

Postgraduate Course.—For N.H.S. principals, April 28 to May 10 at the Welsh National School of Medicine. Details from the secretary of the school, 34, Newport Road, Cardiff.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 17

●HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., Third Dinner Meeting, 8.30 p.m., discussion to be opened by Dr. J. A. Dudgeon and Dr. W. H. Kelleher: Poliomyelitis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 9.30 p.m., Professor A. K. Basu (Calcutta): Clinico-Pathological Study of Cases of Pulmonary Tuberculosis Treated by Antibiotics and Pulmonary Resection. (2) 4 p.m., Dr. K. G. Lowe: Acute Renal Failure.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 5 p.m., public lecture by Dr. J. D. Judah: Oxidative Phosphorylation—(2) Interpretations and Mechanisms.

Tuesday, March 18

B.B.C. TELEVISION.—9.30 p.m., "Your Life in Their Hands," No. 6.—The Ever-Lessening Shadow, from Sully Hospital, Glamorgan.

HEATHERWOOD ORTHOPAEDIC HOSPITAL.—8.30 p.m., Mr. G. P. Arden: Radioactive Isotopes in Orthopaedic Surgery.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann: Microscopical Anatomy of the Ear.

INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor N. F. Maclagan: Biochemistry of Coma. (Postponed from March 4.)

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. K. I. Nissen: Orthopaedic Aid for Spastic States.

Wednesday, March 19

EUGENICS SOCIETY.—At Royal Society, Burlington House, Piccadilly, W., 5.30 p.m., symposium: New Human Demands in Industry. Speakers, Mr. A. Rodger, The Hon. Michael Layton, Mr. R. Peddie, and Dr. K. Hutton, D.Phil.

FACULTY OF ANAESTHETISTS: ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Joseph Clover Lecture by Professor W. D. M. Paton, F.R.S.: Mechanisms of Transmission in the Central Nervous System.

HARVEIAN SOCIETY OF LONDON.—8.15 p.m., Harveian Lecture by Professor Robert Kark (Illinois): Bright's Disease Then and Now.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. E. F. Chin: Indications for and Results of Surgery in Funnel Chest and Congenital Sternal Prominence.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. D. Fergusson: Control of Advanced Cancer.

MIDLAND MEDICAL SOCIETY.—At Dudley Road Hospital, Birmingham, 8.15 p.m., clinical meeting.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. R. Winston Evans: Certain Aspects of the Pathology of Ovarian Tumours.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. A. C. Boyle: Role of the Disk in Backache.

WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, 8.45 p.m., Mr. T. Holmes Sellors: Surgery of the Oesophagus.

Thursday, March 20

BRISTOL UNIVERSITY.—At Large Physics Lecture Theatre, Royal Fort, 8.30 p.m., Patrick Watson Williams Memorial Lecture by Mr. T. E. Cawthorne: Facial Palsy.

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Presidential Address by Dr. L. F. Lamerton, M.Sc., Ph.D.: Examination of the Clinical and Experimental Data Relating to Possible Hazard to the Individual of Small Doses of Radiation.

FOUNTAIN HOSPITAL.—5.30 p.m., subject: Neural Malformations. Papers by Dr. I. W. Millen and Dr. D. H. M. Woollam: Experimental Production of Malformations of the Brain; Dr. L. Crome: Gross Neural Malformations in Mental Defectives.

HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Sir James Paterson Ross.

HYPNOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., annual general meeting. Discussion to be opened by Dr. T. F. Main and Dr. D. E. R. Kelsey: Agoraphobia.

LIVERPOOL MEDICAL INSTITUTION.—3 p.m., Dr. P. H. Whitaker and others: radiological demonstration.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8 for 8.30 p.m., annual general meeting. Discussion: The Problems of Young Married Medical Women.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Sir Reginald Watson-Jones: Physical and Psychological Problems in Orthopaedic Cases.

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 7.45 for 8 p.m., Dr. J. A. Lee: Some Experiences with Extradural Analgesia.

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., 2.30 p.m., meeting.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Ophthalmic Lenses and Their Effects.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Royal Army Medical College, Millbank, S.W., 7.30 p.m., laboratory meeting.

●WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Star and Garter Hotel, Putney Bridge, W., 7.30 for 8 p.m., dinner meeting. Mr. A. Dickson Wright: Famous Operations in History.

WEST OF ENGLAND CHILD HEALTH GROUP.—At Ham Green Isolation Hospital and Sanatorium, Pill, near Bristol, 6.30 p.m., clinical meeting, by invitation of Dr. J. Macrae.

Friday, March 21

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 4.45 p.m., Dr. J. F. Loutit, Dr. A. S. McLean, and Dr. J. D. Abbatt: Medical Problems Associated with Applied Atomic Energy.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., clinical discussion for general practitioners, Mr. G. H. Howells: Cancer of the Larynx.

LEICESTER CHRISTIAN MEDICAL ASSOCIATION.—At Leicester Royal Infirmary, 8.30 for 8.45 p.m., Dr. E. F. Griffith: Psychotherapy and Marital Disharmony.

ROYAL INSTITUTION.—9 p.m., Woodhull Lecture by Professor C. D. Darlington, D.Sc., F.R.S.: Control of Evolution in Man.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Stobhill Hospital, Springburn, Glasgow, 8.30 p.m., clinical night.

Saturday, March 22

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Savoy Hotel, 6.45 p.m. to 1 a.m., annual dinner dance.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Alexander.—On February 17, 1958, at the City General Hospital, Sheffield, to Susan Lilias (formerly Munro), and Conel Alexander, M.B., M.R.C.P., a daughter.

Evans.—On February 4, 1958, at St. Bartholomew's Hospital, London, E.C., to Muriel, wife of Robert J. Evans, M.D., a son—Miles Liddiard.

Evans.—On February 23, 1958, at Morfa New Park Road, Holyhead, Anglesey, to Dr. Joan Evans (formerly Wilson), and Dr. Emrys Evans, a brother for David and Philip.

DEATHS

Smith.—On February 21, 1958, in hospital, Reginald Hubert Smith, F.R.C.S.Ed., D.L.O., of Mawden, Wood End Lane, Stalybridge, Cheshire, aged 57.

Sprunt.—On February 15, 1958, at 35, Castle Terrace, Berwick-on-Tweed, William Rodger Sprunt, T.D., M.B., Ch.B., aged 63.

Wilkes.—On February 12, 1958, in the Birmingham General Hospital, Addie Wilkes, M.R.C.S., L.R.C.P., of 41, Birmingham Road, Great Barr, Staffs, late of Pelsall, Staffs.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Treatment of Paralysis Agitans

Q.—*Is there any progress in the treatment of paralysis agitans?*

A.—There is no progress in the treatment of paralysis agitans, except that there are now several drugs available for controlling the symptoms. For example, rigidity is said to be controlled best by any of the following: benzotropine atropine, benzhexol, and cycrimine. On the other hand, tremor is best controlled by hyoscine, lethargy is best counteracted by amphetamine, and oculogyria by benzhexol. Other effective drugs are ethopropazine and procyclidine, which are included in *New and Non-official Remedies*, 1957. The substance orphenadrine, which is a near relative of diphenhydramine, is said to increase the effectiveness of benzhexol and several other drugs, giving excellent results for short periods but losing its action after a few weeks or months. The papers by L. J. Doshay[1,2] should be consulted.

Perhaps the most important point is that any one drug may have one effect in one patient and a greater effect in a second; in particular the side-effects vary, and consequently many different combinations of drugs can be tried until the optimal combination for each patient is found. Doshay also emphasizes the importance of physiotherapy and psychotherapy.

REFERENCES

[1] Doshay, L. J., *J. Amer. med. Ass.*, 1954, **154**, 680 and 1334.
[2] —— ibid., 1957, **163**, 1352.

Veiling with Contact Lenses

Q.—*I have recently noticed that after wearing my contact lenses for 2 to 4 hours I see coloured rings around bright lights: the phenomenon persists for a short while after removing the lenses. What is the cause?*

A.—This appears to be a case of veiling. If that is so the coloured rings round bright lights are due to superficial oedema of the cornea within the pupillary pencil of light rays. The contact lens is exerting a slight "cupping glass" effect. The degree of veiling described is not serious, does not imply any rise in tension in the eye, and in some cases disappears after a time. Most contact lens wearers may find a trace of this phenomenon if they look for it under appropriate conditions. If veiling increases as time goes on, or if it persists for more than 20 minutes after the lenses are removed, the contact lenses may have to be modified.

Alternatively, the condition described may be due to mucus (true conjunctivitis or allergic response), the position of a bubble under the lens, or, indeed, to true glaucoma. The query illustrates very well the desirability of competent ophthalmic supervision of contact lens cases.

Pili Incarnati

Q.—*What is the treatment for pili incarnati in a young man, and will the condition tend to regress with age?*

A.—Pili incarnati result from a developmental irregularity, the hair follicle being placed obliquely in the skin. The only successful treatments are those which are designed with this anatomical abnormality in mind. The usual method is to free the offending hairs with a needle and then remove them with tweezers. In some cases very close shaving is enough to keep the condition in check. It commonly happens that the pustules are mistaken for those due to chronic infection, but the application of antiseptics and antibiotics is useless. Some authorities advocate *x*-ray epilation, but the effect of this is probably always only temporary, and, of course, the treatment cannot be indefinitely repeated. The only other way of permanently removing these hairs is with electrolysis or diathermy, in the same way as is used for superfluous hairs on the face in women. The disorder does not regress with age, and, if this patient is seriously troubled, epilation by electrolysis should be considered.

Epidermolysis Bullosa

Q.—*How is epidermolysis bullosa inherited?*

A.—The inheritance of epidermolysis bullosa varies according to the type, of which there are several.

(1) Simple epidermolysis bullosa, which appears in the first year of life, is a little more common in males than females. Bullae occur more frequently in hot weather and are provoked by trauma, so that fingers, knuckles, knees, ankles, and toes are usually affected but only rarely the buccal mucosa. On healing, no scars remain and no epidermal cysts. The condition is inherited as a dominant characteristic.

(2) Recurrent bullous eruption of the feet is similar to the above, but the bullae occur usually only on the feet and only in hot weather. It is not simply a mild form of (1), as it is regularly transmitted in this form as a dominant characteristic without variations to (1) in certain members of the family.

(3) Dystrophic hyperplastic epidermolysis bullosa. Traumatic bullae may appear soon after birth or in infancy or not until puberty. Mucous membranes are affected in about a fifth of the cases, and bullae (sometimes haemorrhagic) may appear after the slightest injury, most commonly on the head and limbs. Scarring, keloid formation, epidermal cysts, and dystrophy of the nails may follow. Hyperplastic conditions such as ichthyosis, palmar or plantar keratoses, hypertrichosis, etc., may be present. The condition is inherited as a dominant characteristic.

(4) Dystrophic hypoplastic epidermolysis bullosa is similar to (3), though bullae may arise apparently spontaneously and death occurs early in life. There are, moreover, certain hypoplastic abnormalities which may occur with this condition—absent or rudimentary nails, thin dry skin, malformation of teeth, etc. It is inherited as a recessive characteristic.

(5) Epidermolysis bullosa hereditaria letalis is similar to and a variant of (4). Death occurs *in utero* or during the first few months of life. It is inherited as a recessive characteristic.

Oral Anticoagulants and Surgical Haemorrhage

Q.—*Is there any danger of bleeding when operating on a patient who is being given phenindione and whose prothrombin time is 30 seconds?*

A.—Operation on a patient within the first four hours after giving a single dose of phenindione is not accompanied by risk of haemorrhage, since the anticoagulant effect is not maximal for some 18–26 hours after ingestion. When the prothrombin level has been depressed, however, there is always an increased tendency to bleed, though with a patient whose prothrombin time is 30 seconds (assuming the control normal prothrombin time is 14 seconds with the technique used), the risk of uncontrollable haemorrhage is not great. The nature of the operation must, however, also be taken into account; in a superficial or straight operation, where bleeding points can be controlled individually, severe haemorrhage is unlikely when the prothrombin time is 30 seconds, but in an operation which involves stripping or denuding a large area (as for example with abdominal adhesions) and where there are multiple uncontrolled bleeding points, oozing haemorrhage is considerably enhanced even with "low grade" anticoagulant therapy. All risk of haemorrhage may, however, be removed by the administration of vitamin K_1 to cases where an emergency operation must be performed while the patient is on an oral anticoagulant drug. Its action is maximal about two hours after administration.

Treatment of Gout

Q.—*Is demecolcine a better treatment for gout than colchicine?*

A.—Colchicine is a highly effective specific remedy in *acute* attacks of gout, and it is recommended that small doses (0.5–2 mg. daily) should be given continuously to prevent the recurrence of attacks.[1] The mechanism of its action is not known. It does not affect uric acid metabolism. Its only drawback is that it nearly always causes acute gastro-intestinal irritation with diarrhoea and loss of appetite.

Demecolcine (desacetylmethylcolchicine), which was isolated from *Colchicum autumnale* in 1950[2] was found to have a very much lower general toxicity than colchicine in several animal species.[3] It is reported to control acute attacks of gout as effectively as colchicine, without producing gastro-intestinal disturbances (dose 1–5 mg. daily).[4 5] It is, however, an extremely toxic substance, and its apparent non-toxicity when it is first taken has led to the administration of dangerously high doses. A macropapular eruption developed on a dose of 8 mg. daily.[5] Total alopecia resulted from the administration of 14 mg.[6] A patient with follicular lymphoma who was apparently well able to tolerate 4 mg. daily suddenly developed a maculopapular rash which spread over the entire body; there was also ulceration and swelling of the mucous membrane which made swallowing impossible. This patient recovered after about two months, but total alopecia ensued. Another patient with chronic granulocytic leukaemia, taking 5–10 mg. daily, suddenly became gravely ill with a severe fall in all blood counts.[7]

Three cases of agranulocytosis are also reported.[8] In one of these the patient was given 8 mg. in eight hours for an acute attack of gout, and was so pleased with the prompt relief and absence of side-effects on the first day that he repeated the treatment for four more days, taking 39 mg. in five days.

In chronic gout, probenecid, 0.5–1 g. twice daily, should be given as well as colchicine.[1] This substance selectively inhibits the resorption of urates from the renal tubules and increases urate excretion by 30–200%. It should be given continuously, as its withdrawal may precipitate an acute attack. Its effect is nullified if aspirin or salicylates are taken at the same time. Probenecid is the treatment of choice for chronic gout, colchicine being reserved for acute attacks.

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Rh Sensitization from Polio Vaccination

Q.—*What steps have been taken to eliminate or minimize the risk of rhesus sensitization following the use of poliomyelitis vaccine in rhesus-negative persons? What experimental evidence is there that the vaccine does not sensitize?*

A.—The Rh antigens, which are reported to be almost insoluble, form part of the monkey cellular material in the original tissue culture. As the protein content of the final vaccine is very low and must not be greater than a certain percentage, it is likely that nearly all of the cellular detritus is removed during the purification of the vaccine. It is also stated that the Rh antigens in the monkey are slightly different from those in man.[1]

The Francis report[2] quotes the evidence of two independent workers that 32 immunized children and 2 laboratory workers who were Rh negative did not show Rh or Hr antibodies in their sera after immunization. Abelson *et al.*,[3] working in Philadelphia, found no Rh antibodies in the sera vaccine. They inoculated vaccine into groups of Rh negative adults who had been sensitized to Rh antigens either by blood transfusion, pregnancy, or the repeated injection of Rh-positive blood. In one group a small rise in titre of Rh antibody was observed following vaccination with a particular batch of vaccine in seven of eight persons whose serum contained antibodies before inoculation. None of the 16 other persons inoculated with two other batches of vaccine showed a rise in antibodies to Rh antigens. The authors concluded that the rise in antibodies observed in the one group of sensitized persons was an anamnestic response. Repeated inoculation of Salk vaccine at weekly intervals for two months was carried out in five Rh-negative volunteers. No Rh antibodies were found after this procedure, nor did a single subsequent inoculation of Rh-positive blood cause an appearance of agglutinins such as would have indicated that the vaccine had sensitized the persons to the Rh antigen. It was considered that the vaccine does not sensitize Rh-negative persons.

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Penicillin-resistant Gonorrhoea

Q.—*What treatment is indicated in the case of a married couple whose bacteriologically confirmed gonorrhoea has failed to respond to penicillin?*

A.—Cases of gonorrhoea resistant to penicillin appear to be on the increase. In such cases one injection of streptomycin 1 g. or terramycin 0.5 g. 6-hourly for two or three days is usually effective. Both patients should be treated on the same day. No special investigations are considered necessary.

Spleen and Antibody Formation

Q.—*Does the absence of the spleen affect a person's response to active immunization?*

A.—The spleen certainly plays some part in antibody formation, but there are other sources of antibody, the lymph glands being perhaps the most important. There is no reason to believe absence of the spleen will materially affect the response to active immunization.

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